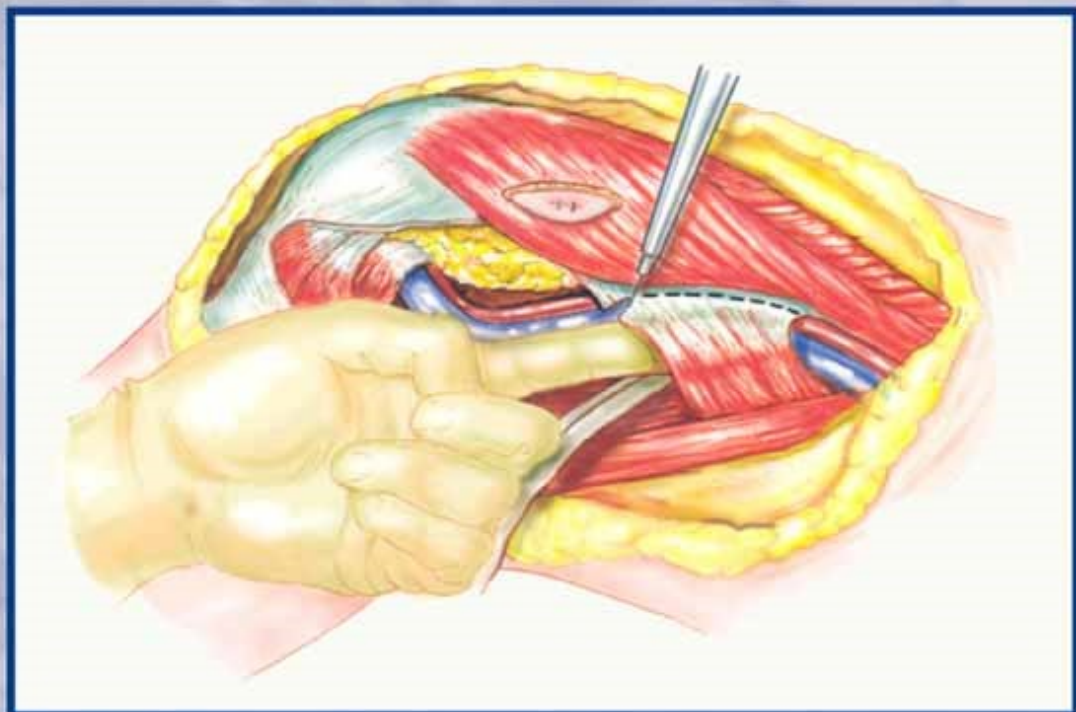


WASHINGTON CANCER INSTITUTE

Musculoskeletal Cancer Surgery

Treatment of Sarcomas and Allied Diseases

Martin M. Malawer and Paul H. Sugarbaker



Kluwer Academic Publishers

Musculoskeletal Cancer Surgery

**Treatment of Sarcomas and
Allied Diseases**



The Washington Hospital Center (WHC), National Rehabilitation Hospital and National Children's Hospital are located due north of the U.S. Capitol Building in Washington, D.C. These combined institutions are uniquely qualified to treat and rehabilitate patients with musculoskeletal cancer.

Musculoskeletal Cancer Surgery

Treatment of Sarcomas and Allied Diseases

Authors

Martin Malawer, M.D.

*Washington Cancer Institute,
Washington Hospital Center,
Washington, D.C., USA*

Paul H. Sugarbaker, M.D.

*Washington Cancer Institute,
Washington Hospital Center,
Washington, D.C., USA*

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Foreword

Steven A. Rosenberg, MD

In the past two decades significant progress has occurred, in the management of patients with musculoskeletal cancers, that has improved both the survival and the quality of life of afflicted patients. Changes in the management of these patients have mirrored trends in the entire field of oncology.

The most significant change has been improvement in the surgical techniques for the resection of musculoskeletal cancers based on a detailed understanding of the anatomic features of each particular tumor site, as well as an appreciation of the natural biology that affects the local spread of these tumors. The current volume of *Musculoskeletal Cancer Surgery: Treatment of Sarcomas and Allied Diseases* provides a detailed description of important changes in the surgical approach to these patients. Amputation, once the mainstay of treatment for patients with bony and soft-tissue extremity sarcomas, has now largely been replaced by limb-sparing surgery using innovative approaches to cancer resection and the advent of new reconstruction techniques that can restore function in ways not possible even a decade ago. Although debilitating amputations are still required for some patients with locally extensive cancers, most patients with these tumors can look forward to surgical procedures that will maximize their functional outcome. The sophistication of many of these limb-sparing surgical approaches has resulted in a shift in the expertise required to perform these procedures and, increasingly, specialists in the management of musculoskeletal tumors have arisen to provide these patients with the benefits of these advances.

A second change in the management of these patients has been the introduction of combined-modality treatment utilizing the concerted application of surgery, radiation therapy and chemotherapy in a carefully integrated fashion to maximize survival and

quality of life. The use of local radiation therapy has had a profound impact on the ability to achieve local control. Cooperation between surgeons and radiation therapists often results in the tailoring of surgical procedures to maximize the combined application of these two effective treatment modalities. Although impact on overall survival has not been demonstrated due to the addition of radiation therapy, important advances in improving the quality of life of patients receiving this combined-modality treatment have been evident.

A third change impacting on the survival of patients with musculoskeletal cancers has been the aggressive resection of metastatic deposits. Surgery remains the most effective treatment for adult patients with limited metastatic cancer, and durable disease-free and overall survival can be achieved by the vigorous resection of metastases arising from these cancers. Although the use of adjuvant chemotherapy has had dramatic impact on the treatment of many musculoskeletal cancers in children, the impact of chemotherapy on adults remains a controversial issue. Although transient responses can be seen in adults with many types of soft-tissue sarcomas, they are very rarely curative and the development of more effective systemic treatments for patients with soft-tissue sarcomas remains a major challenge in the future treatment of patients with this disease.

The state-of-the-art surgical techniques described in this text, applied in the context of integrated cancer therapy, can provide great benefit to patients with musculoskeletal cancers.

*Chief, Surgery Branch,
National Cancer Institute,
National Institutes of Health,
Bethesda, Maryland*

Acknowledgements

Martin Malawer, MD

Halstead once stated that "the operating room was the laboratory for the surgeon". This is as true today as it was a century ago. The surgical techniques described in this textbook were developed over a course of 20 years in the treatment of over 4000 patients. We would like to acknowledge our patients for their belief in us as surgeons and in our ability to restore the function to their extremities in lieu of an amputation. For those patients who did require an amputation, we acknowledge the tremendous will that they have had.

Surgery and surgical training is a three-way communication between patients, fellows and senior surgeons. This spoken and unspoken dialogue has been the foundation of many of these concepts, ideas and motivations presented in this textbook. We would like to acknowledge all of the residents and fellows that we have trained.

This textbook would not exist without the outstanding artistic skills of Joyce Hurwitz. Mrs Hurwitz has spent 20 years in close cooperation with the senior authors, illustrating multiple publications, presentations, posters and textbooks. Her utmost knowledge of surgical anatomy, combined with her interest and motivation in participating within the scientific community, sets her apart as a truly gifted individual.

Finally, the authors would like to acknowledge the hard work and dedication of all of the contributors. We are especially appreciative of the long hours and days that our Senior Research Assistant, Kristen Kellar, has spent, without which this book never would have been completed.

Dedication: To Ralph C. Marcove, MD and Kenneth C. Francis, MD

Martin Malawer, MD

Prior to the early 1970s almost all bone sarcomas were treated by amputation. Two surgeons in the United States, both in New York City, began the specialty of limb-sparing surgery as we know it today. Dr Kenneth C. Francis (photo not available) was the Clinical Professor of Orthopedic Surgery at the New York University School of Medicine. He was also the first orthopedic surgeon to be the chief of the Bone Tumor Service at Memorial Sloan Kettering Cancer Center. His first and only fellow was Dr Ralph Marcove, who ultimately became chief of the Bone Tumor Service at Memorial Sloan Kettering Cancer Center. Although separated by only one mile in New York City, the two men independently performed and developed the original techniques of distal femoral resections, total femoral prosthetic replacements, shoulder girdle resections, scapular resections and pelvic resections. The early 1970s yielded the introduction of Adriamycin® and methotrexate. Both surgeons understood the significance of adjuvant chemotherapy and the impact that it would have on patient survival and the choice of surgical procedure. The subsequent studies at Memorial Sloan Kettering Cancer Center, T1–T10, were undertaken by a team of oncologists with Dr Marcove as the surgeon. In 1973 Dr Francis performed the first distal femoral resection and reconstructed the defect at that time with a long-stemmed Walldius prosthesis. This, to the author's knowledge, was the first distal femoral replacement performed in the United States, if not the world. He attended a meeting at what was then a small company in New Jersey, Howmedica, Inc., and sat down with their engineers and outlined on a napkin a distal femoral prosthesis with a long femoral and tibial stem with a Walldius hinge. This book is dedicated to the knowledge, insightfulness and teaching and surgical skills of these two men. Dr Kenneth Francis died prematurely in May 1976, at the age of 53. Dr Ralph Marcove retired from Columbia Presbyterian Hospital in 1999 and died in February 2000.



Dr Ralph Marcove

Preface

Martin Malawer, MD

Musculoskeletal cancer surgery has undergone dramatic changes within the past two decades. Limb-sparing surgery is the hallmark of the surgical advances developed by this specialty. The role of the orthopedic oncology surgeon in the 1970s was to perform high-level amputations. This is what distinguished the orthopedic cancer surgeon from the general orthopedic surgeon. The development of limb-sparing surgery, in conjunction with the dynamic advances in imaging and chemotherapy, created the specialty of musculoskeletal oncology. The operative procedures performed today barely existed two decades ago. Today, approximately 90–95% of all bone and soft-tissue sarcomas can be treated by limb-sparing surgery. The aim of this book is to present in a concise, organized and well-illustrated format, the surgical techniques involved with limb-sparing procedures of the entire musculoskeletal system, including the upper and lower extremities as well as the pelvic and shoulder girdle. These techniques are a combination of surgical procedures that used to be considered of interest only to the general surgeon, vascular surgeon, plastic surgeon and orthopedic surgeon. The development of these multiple-treatment strategies and techniques has created the field of musculoskeletal cancer surgery as we know it today.

The surgical experience of the two authors, Martin Malawer, MD, and Paul H. Sugarbaker, MD, spans more than two decades each. The combined experience of Dr Malawer, Professor of Orthopedic Surgery at George Washington University, Children's National Medical Center, and the Washington Cancer Institute Division of Orthopedic Oncology, and Dr Sugarbaker, who developed several of the techniques described in this book while at the National Cancer Institute, Bethesda, Maryland, forms the foundation for this book. The techniques described in these pages have been developed by both authors over the past two decades.

The aim of this textbook is to illustrate well a step-by-step approach to limb-sparing procedures of the musculoskeletal system. These techniques, although not unique, are described specifically from the authors' experience, which began in the early 1970s and continues today. Dr Malawer has extensively reported

different techniques for limb-sparing resections and endoprosthetic reconstructions. The technique of allograft replacement was developed in the early 1970s and utilized widely until the 1980s. Such techniques are not utilized by the authors but are well described elsewhere.

Surgery is a visual field, and the surgeon works in three dimensions. Therefore, the majority of the contents of this book are accompanied by photographs and illustrations of the surgical procedure as well as preoperative studies that the authors feel are uniquely important. The surgical descriptions, anatomic depictions, and the significance of each imaging study to each operative procedure are emphasized.

Since the mid-1970s the two authors have provided surgical care for approximately 4000 patients with benign, malignant and metastatic lesions, in children and adults. Detailed files, including operative photographs, pathology slides, Kodachrome slides and slides of the significant imaging studies for all of the major cases have been kept on each operative procedure. This collection is housed at the Center for Orthopedic Oncology and Musculoskeletal Research at the Washington Cancer Institute and is available to American and international surgeons and oncologists for study and research purposes.

Despite the complexity of limb-sparing surgical procedures and the multiple imaging studies, it was the purpose of the authors to present these data in a simple visual format. The bibliography is limited in most chapters, because the techniques described were developed by the authors themselves. The general chapters are well-referenced with the most up-to-date citations.

This book contains 36 chapters, divided into four sections. It addresses the basic pathology, surgical technique and management of all extremity and pelvic and shoulder girdle tumors as well as abdominal and truncal sarcoma surgery.

Chapter 1 includes a discussion of bone and soft-tissue sarcomas, including their epidemiology, radiographic characteristics and pathology. Biopsy techniques are discussed in Chapter 2. In Chapter 3, chemotherapy is discussed, outlining the chemotherapeutic agents that are effective in the treatment of bone and soft-tissue

sarcomas. Dr Dennis Priebat details the chemotherapy strategy that has evolved over the past 20 years. The experience of isolated-limb perfusion, a new technique used to treat sarcomas, is described in Chapter 4. Dr Brian Fuller, Chief of the Radiation Oncology Branch at the National Cancer Institute, in Chapter 5, describes the most current and comprehensive strategy for radiation therapy for extremity sarcomas. Chapter 6 discusses the use of cryosurgery in the treatment of certain bone tumors. This technique was developed by Dr Ralph Marcove at Memorial Sloan Kettering Cancer Center and has been continued by the authors. Chapters 7 and 8 summarize the management of abdominal and pelvic sarcomas. The author, Dr Paul Sugarbaker, has uniquely developed many techniques over the past 25 years. Chapters 9, 10 and 11 provide overviews of the treatment of tumors of the shoulder girdle, pelvic girdle and metastatic bone tumors, respectively. These chapters lay the foundation for the specific limb-sparing procedures in the remaining portion of the textbook.

Section Two describes in detail the techniques for muscle group resections of the lower extremity including gluteus maximus, adductor muscle group, quadriceps muscle group, posterior thigh and popliteal space.

Section Three discusses the surgical amputations utilized in orthopedic oncology surgery. These tend to be high-level amputations with which orthopedic and general surgeons tend not to be familiar. Forequarter amputation and the various types of hemipelvectomy are described. Dr Sugarbaker developed the technique of an anterior myocutaneous flap for patients with massively contaminated pelvic and

buttock structures that cannot be resected by the standard posterior flap hemipelvectomy. These operative procedures were often deemed difficult and radical, but are still used today to cure certain patients who cannot be treated by limb-sparing surgeries. Phantom pain, a complication following an amputation for cancer patients, is discussed in Chapter 24. Due to the neuropathic effects of the chemotherapeutic agents, as well as the young age of these patients, this problem occurs frequently. Dr Lee Ann Rhodes describes treatment considerations for phantom limb pain.

Section Four describes in detail the limb-sparing procedures around the pelvis, proximal and distal femur, proximal tibia, fibula, proximal humerus and scapula. Although these procedures are performed at many centers throughout the world today, the techniques, morbidity and complications vary tremendously. The techniques as described by Dr Malawer, which he has perfected over the past 20 years, are presented in detail. The required staging studies and unique anatomic considerations, from a surgeon's viewpoint, are outlined for each anatomic site, with special considerations for the evaluation of the imaging studies.

The Appendix includes two chapters of interest to the musculoskeletal surgeon. Appendix A is a description of an abdominoinguinal incision developed by Dr Constantine Karakousis for resection of pelvic tumors. This is a combined intra- and extraperitoneal approach. Canine osteosarcomas are discussed by Dr Charles Kuntz. Osteosarcomas in dogs are extremely common, and the techniques and basis of limb-sparing surgical techniques in dogs offer an excellent orthopedic animal model and are of interest to musculoskeletal cancer surgeons.

Contributors

Jacob Bickels, MD

Attending Surgeon
The National Unit of Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Brian G. Fuller, MD

Senior Investigator
Radiation Oncology Branch
Radiation Oncology Sciences Program
National Cancer Institute

Mordechai Gutman, MD

Director, Surgical Unit of Regional Chemotherapy
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Associate Professor of Surgery
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

Robert M. Henshaw, MD

Department of Orthopedic Oncology
Washington Cancer Institute at
The Washington Hospital Center, Washington, DC
Assistant Clinical Professor of Orthopedic Surgery
George Washington University School of Medicine
Washington, DC
Consultant, Surgery Branch of the National Cancer
Institute
National Institutes of Health
Bethesda, Maryland

Moshe Inbar, MD

Director, Department of Medical Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Associate Professor of Oncology
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

James Jelinek, MD

Chairman, Department of Radiology
Washington Hospital Center, Washington, DC
Visiting Scientist
Department of Radiologic Pathology, Armed Forces
Institute of Pathology, Washington, DC

Constantine P. Karakousis, MD, PhD

Associate Chief
Department of Surgical Oncology
Roswell Park Memorial Institute
Buffalo, New York

Orit Katzir, BOT

The National Unit of Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Kristen L. Kellar, BS

Department of Orthopedic Oncology
Washington Cancer Institute at
The Washington Hospital Center, Washington, DC

Joseph M. Klausner, MD

Chairman of Surgery
Director, Departments of Surgery B and C
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Professor of Surgery
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

Yehuda Kollender, MD

Attending Surgeon
The National Unit of Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Charles Kuntz, DVM, MS

Diplomate of the American College of Veterinary
Surgeons
Chief of Surgery
Regional Veterinary Referral Center
Springfield, VA

Eric Lang, MD

Attending Anesthesiologist
Department of Anesthesiology
Tel-Aviv Sourasky Medical Center
Tel-Aviv, Israel

Dina Lev-Chelouche, MD

Attending Surgeon
Department of Surgery B
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Martin Malawer, MD

Director, Department of Orthopedic Oncology
Washington Cancer Institute at
The Washington Hospital Center, Washington, DC
Professor of Orthopedic Surgery
The George Washington University School of
Medicine
Washington, DC
Consultant, Surgery Branch at the National Cancer
Institute
The National Institutes of Health
Bethesda, Maryland
Clinical Professor of Orthopedic Surgery
Georgetown University School of Medicine
Washington, DC

Nissim Marouani, MD

Attending Anesthesiologist
Acute Postoperative Pain Service
Department of Anesthesiology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Isaac Meller, MD

Director, The National Unit of Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Senior Lecturer
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

David Niv, MD

Director, Pain Service
Department of Anesthesiology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Associate Professor of Anesthesiology
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

Riki Oren, BPT

The National Unit of Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Dennis Priebat, MD

Director of Medical Oncology
Washington Cancer Institute at
The Washington Hospital Center, Washington, DC

Lee Ann Rhodes, MD

Medical Director of Pain Management
Washington Cancer Institute at
The Washington Hospital Center, Washington, DC

Cynthia K. Rubert, MD

Department of Orthopedic Oncology
Washington Cancer Institute at
The Washington Hospital Center
Washington, DC

Valery Rudick, MD

Director, Department of Anesthesiology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Senior Lecturer
Associate Professor of Anesthesiology
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

Barry Shmookler, MD

Director of Surgical Pathology
The Washington Hospital Center
Washington, DC

Paul Sugarbaker, MD

Director, Surgical Oncology
Washington Cancer Institute at
The Washington Hospital Center
Washington, DC

Avi Weinbroum, MD

Director, Post-Anesthesia Care Unit
Department of Anesthesiology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
Lecturer
Sackler School of Medicine, Tel-Aviv University
Tel-Aviv, Israel

James C. Wittig, MD

Assistant Professor of Orthopedic Surgery
Department of Orthopedic Surgery
New York University Medical Center
Hospital for Joint Diseases
Bellevue Hospital Center
New York, New York

Alice Zagury, BPT, MSc

Children's Hospital and the National Unit of
Orthopedic Oncology
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Section 1

Principles of Management

1

Bone and Soft-tissue Sarcomas: Epidemiology, Radiology, Pathology and Fundamentals of Surgical Treatment

**Barry Shmookler, Jacob Bickels, James Jelinek, Paul
Sugarbaker and Martin Malawer**

OVERVIEW

An understanding of the basic biology and pathology of bone and soft-tissue tumors is essential for appropriate planning of their treatment. This chapter reviews the unique biological behavior of soft-tissue and bone sarcomas, which underlies the basis for their staging, resection, and the use of appropriate adjuvant treatment modalities. A detailed description of the clinical, radiographic, and pathological characteristics for the most common sarcomas is presented.

BIOLOGY AND NATURAL HISTORY OF BONE AND SOFT-TISSUE TUMORS

Soft-tissue and bone sarcomas are a rare and heterogeneous group of tumors. Although soft tissues and bone comprise 75% of the average body weight, these neoplasms represent less than 1% of all adult and 15% of pediatric malignancies. The annual incidence in the United States, which remains relatively constant, is approximately 6000–7000 soft-tissue and 2500 bone sarcomas. Because these lesions are so rare, few pathologists have sufficient experience to deal comfortably with their diagnosis. This is further compounded by the steady evolution in the classification of soft-tissue and bone tumors, which is based on their biological behavior, ultrastructure, and results of immunohistochemical and cytogenetic studies.

Risk factors for soft-tissue and bone sarcomas include previous radiation therapy, exposure to chemicals (e.g., vinyl chloride, arsenic), immunodeficiency, prior injury (scars, burns), chronic tissue irritation (foreign-body implants, lymphedema), neurofibromatosis, Paget's disease, bone infarcts, and genetic cancer syndromes (hereditary retinoblastoma, Li–Fraumeni syndrome, Gardner's syndrome). In most patients, however, no specific etiology can be identified.

Sarcomas originate primarily from elements of the mesodermal embryonic layer. Soft-tissue sarcomas are classified according to the adult tissue that they resemble. Similarly, bone sarcomas are usually classified according to the type of matrix production: osteoid-producing sarcomas are classified as osteosarcomas, and chondroid-producing sarcomas are classified as chondrosarcomas. The three most common soft-tissue sarcomas are malignant fibrous histiocytoma (MFH), liposarcoma, and leiomyosarcoma. These tumors are anatomic site-dependent; in the extremities the common subtypes are MFH and liposarcoma, whereas liposarcomas and leiomyosarcoma are the common subtypes in the retroperitoneum and the abdominal cavity. The most common bone sarcomas are osteosarcoma, chondrosarcoma, and Ewing's sarcoma.

Although soft-tissue sarcomas can arise anywhere in the body, the lower extremities are the most common site. Incidence is as follows: lower extremities – 46%; trunk – 19%; upper extremities – 13%; retroperitoneum – 12%; head and neck – 9%; other locations – 1%. The presenting symptoms and signs of soft-tissue sarcomas are nonspecific; they commonly present as a painless, slow-growing mass. Diagnosis of sarcomas involving the abdominal and pelvic cavity is subtle; these tumors may progress for long periods without causing overt symptoms. Their location deep within the body precludes palpation of the tumor mass early in the course of the disease; consequently, these tumors often reach tremendous size prior to diagnosis.

In the past two decades, survival and the quality of life of patients with soft-tissue and bone sarcomas have dramatically improved as a result of the multimodality treatment approach. Surgery, used in combination with chemotherapy and radiation therapy, can achieve cure in the majority of patients with soft-tissue and bone sarcomas and resection is performed in lieu of amputation in more than 90% of all patients. Principles of chemotherapy and radiation therapy in the treatment of soft-tissue and bone sarcomas are discussed in Chapters 3, 4, and 5.

Biological Behavior

Tumors arising in bone and soft tissues have characteristic patterns of biological behavior because of their common mesenchymal origin and anatomical environment. Those unique patterns form the basis of the staging system and current treatment strategies. Histologically, sarcomas are graded as low, intermediate, or high grade. The grade is based on tumor morphology, extent of pleomorphism, atypia, mitosis, and necrosis. It represents its biological aggressiveness and correlates with the likelihood of metastases.

Sarcomas form a solid mass that grows centrifugally with the periphery of the lesion being the least mature. In contradistinction to the true capsule that surrounds benign lesions, which is composed of compressed normal cells, sarcomas are generally enclosed by a reactive zone, or pseudocapsule. This consists of compressed tumor cells and a fibrovascular zone of reactive tissue with a variable inflammatory component that interacts with the surrounding normal tissues. The thickness of the reactive zone varies with the histogenic type and grade of malignancy. High-grade sarcomas have a poorly defined reactive zone that may be locally invaded by the tumor ([Figure 1.1](#)).

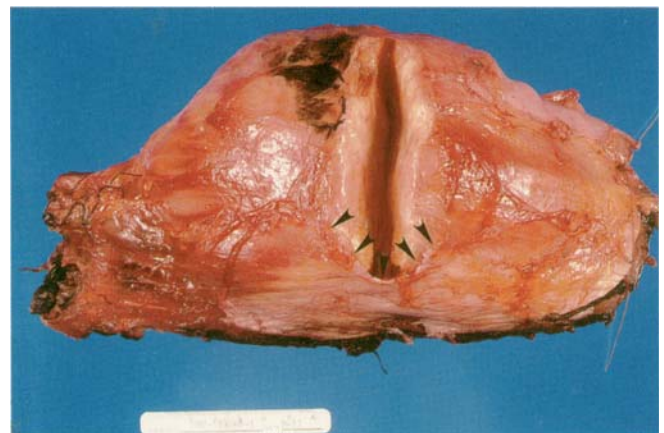


Figure 1.1 A pseudocapsule of a high-grade soft-tissue sarcoma (arrows). It is composed of compressed tumor cells and a fibrovascular zone of reactive inflammatory response.

In addition, they may break through the pseudocapsule to form metastases, termed "skip metastases", within the same anatomical compartment in which the lesion is located. By definition, these are locoregional micrometastases that have not passed through the circulation (Figure 1.2). This phenomenon may be responsible for local recurrences that develop in spite of apparently negative margins after a resection. Although low-grade sarcomas regularly interdigitate into the reactive zone, they rarely form tumor skip nodules beyond that area.

Sarcomas respect anatomical borders. Local anatomy influences tumor growth by setting natural barriers to extension. In general, sarcomas take the path of least resistance and initially grow within the anatomical compartment in which they arose. In a later stage the walls of that compartment are violated (either the cortex of a bone or aponeurosis of a muscle), and the tumor breaks into a surrounding compartment (Figure 1.3). Most bone sarcomas are bicompartmental at the

time of presentation; they destroy the overlying cortex and extend directly into the adjacent soft tissues (Figures 1.4, 1.5). Soft-tissue sarcomas may arise between compartments (extracompartmental) or in an anatomical site that is not walled off by anatomical barriers such as the intermuscular or subcutaneous planes. In the latter case they remain extracompartmental and only in a later stage break into the adjacent compartment. Carcinomas, on the other hand, directly invade the surrounding tissues, irrespective of compartmental borders (Figure 1.6).

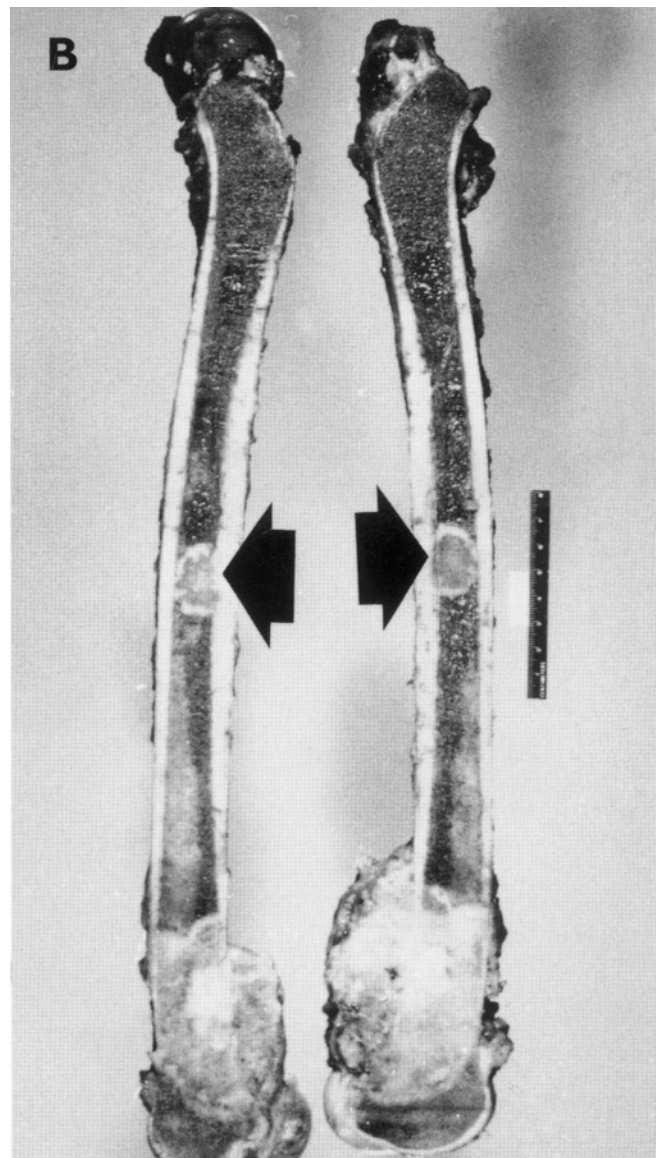
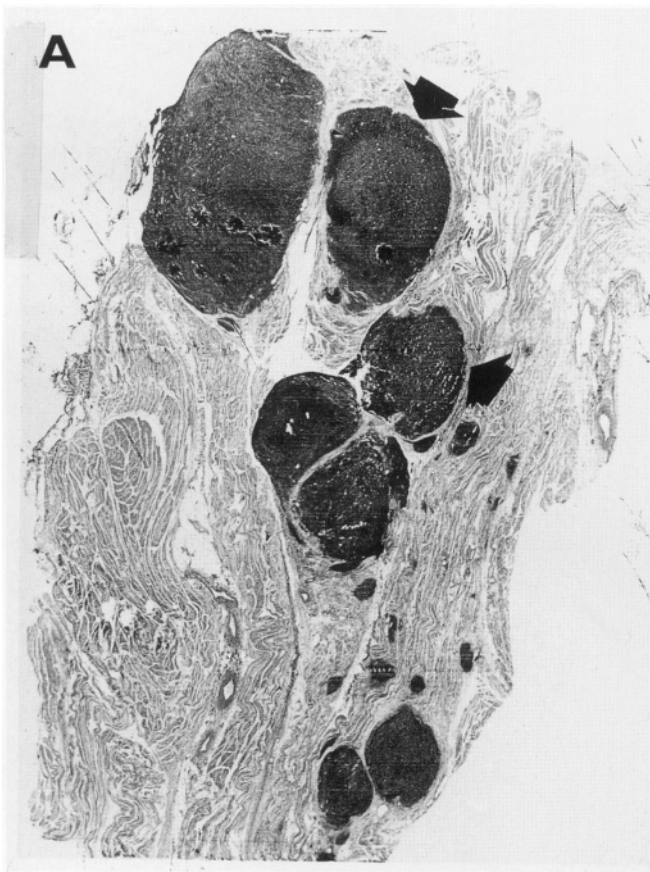


Figure 1.2 High-grade sarcomas may break through the pseudocapsule to form "skip" metastases (arrows) within the same anatomical compartment. They are occasionally found with low-grade sarcomas. Skip nodules are tumor foci not in continuity with the main tumor mass. (A) Multiple satellite nodules (arrows) associated with a high-grade MFH. Note the normal intervening tissue. (B) "Skip" metastases (arrows) from an osteosarcoma of the distal femur. This finding is preoperatively documented in less than 5% of patients.

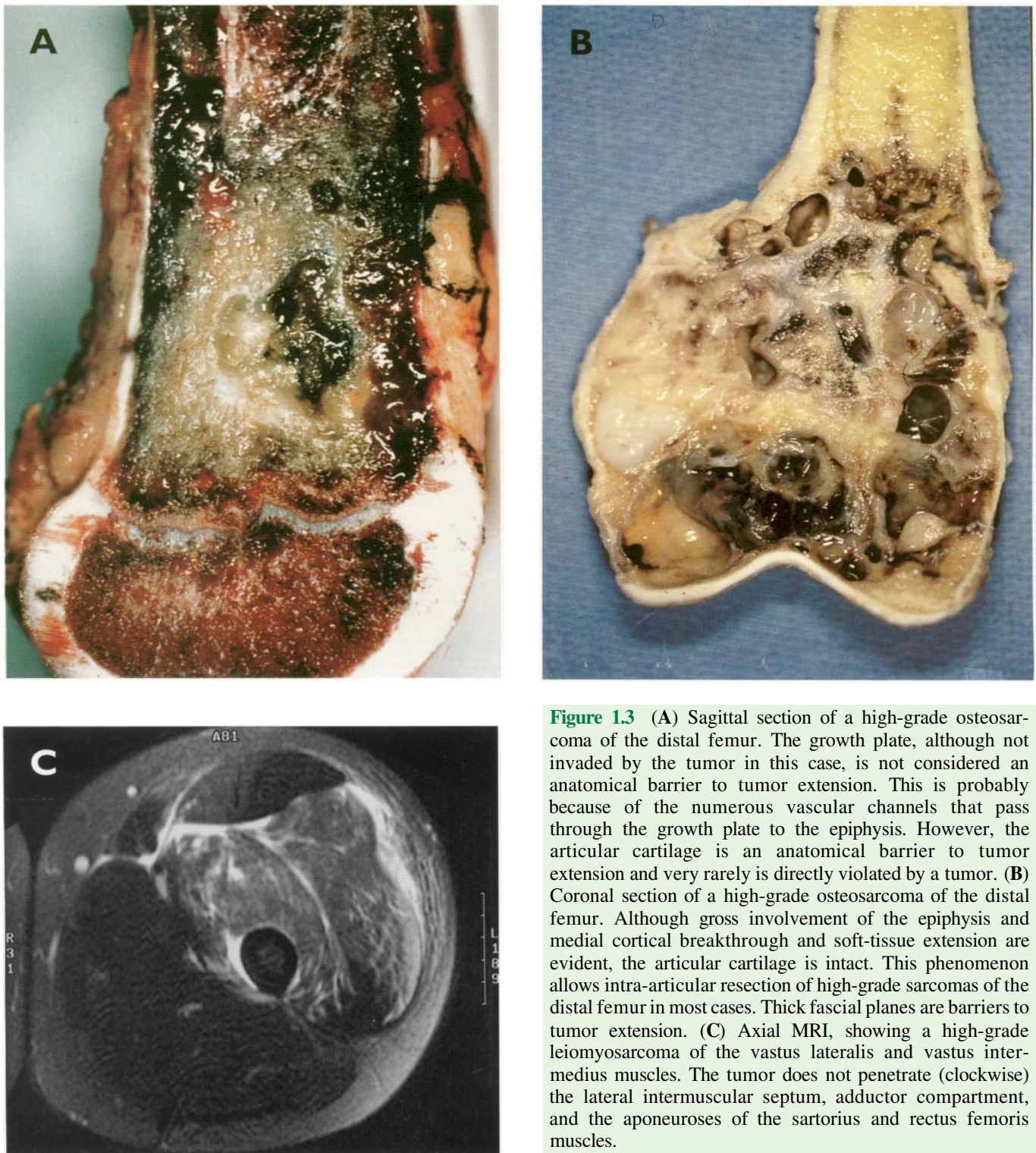


Figure 1.3 (A) Sagittal section of a high-grade osteosarcoma of the distal femur. The growth plate, although not invaded by the tumor in this case, is not considered an anatomical barrier to tumor extension. This is probably because of the numerous vascular channels that pass through the growth plate to the epiphysis. However, the articular cartilage is an anatomical barrier to tumor extension and very rarely is directly violated by a tumor. (B) Coronal section of a high-grade osteosarcoma of the distal femur. Although gross involvement of the epiphysis and medial cortical breakthrough and soft-tissue extension are evident, the articular cartilage is intact. This phenomenon allows intra-articular resection of high-grade sarcomas of the distal femur in most cases. Thick fascial planes are barriers to tumor extension. (C) Axial MRI, showing a high-grade leiomyosarcoma of the vastus lateralis and vastus intermedius muscles. The tumor does not penetrate (clockwise) the lateral intermuscular septum, adductor compartment, and the aponeuroses of the sartorius and rectus femoris muscles.

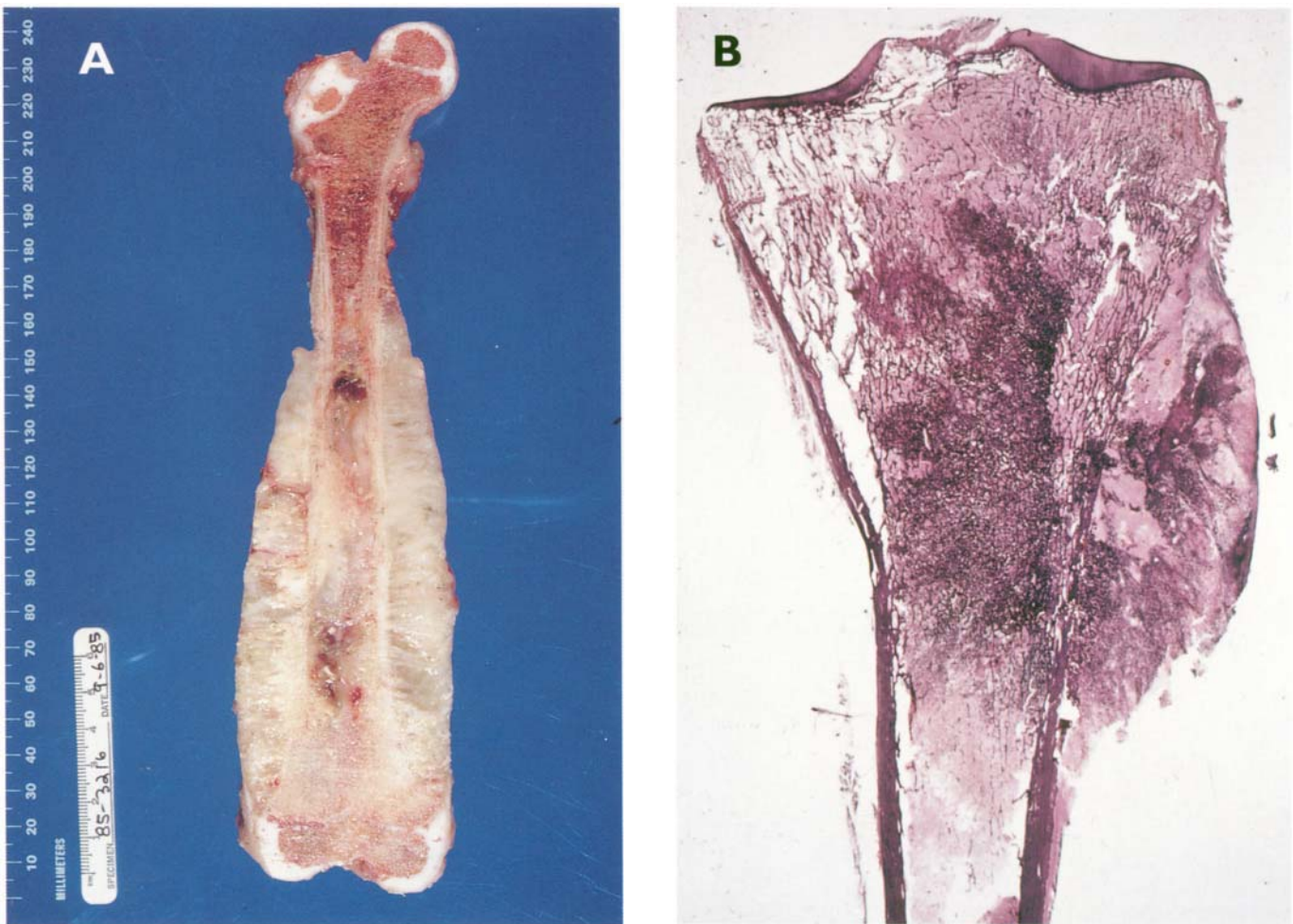


Figure 1.4 (A) Ewing's sarcoma of the distal two-thirds of the femur, and (B) osteosarcoma of the proximal tibia. Note the extraosseous component of the tumor. Most high-grade bone sarcomas are bicompartamental at the time of presentation (i.e., they involve the bone of origin as well as the adjacent soft tissues). Tumors at that extent are staged as IIB tumors (see staging of malignant bone tumors: Enneking's classification).

Joint Involvement

Direct tumor extension through the articular cartilage is rare and usually occurs as the result of a pathological fracture with seeding of the joint cavity or by pericapsular extension (Figure 1.7). Occasionally, structures that pass through the joint (e.g., the cruciate ligaments) act as a conduit for tumor growth (Figures 1.8, 1.9). Transcapsular skip nodules are demonstrated in 1% of all osteosarcomas.

Metastatic Pattern

Unlike carcinomas, bone and soft-tissue sarcomas disseminate almost exclusively through the blood. Hematogenous spread of extremity sarcomas is manifested by pulmonary involvement in the early stages

and by bony involvement in later stages (Figure 1.10). Abdominal and pelvic soft-tissue sarcomas, on the other hand, typically metastasize to the liver and lungs. Low-grade soft-tissue sarcomas have a low (< 15%) rate of subsequent metastasis while high-grade lesions have a significantly higher (> 15%) rate of metastasis. Metastases from sarcomas to regional lymph nodes are infrequent; the condition is observed in only 13% of patients with soft-tissue sarcomas and 7% of bone sarcomas at initial presentation. The prognosis associated with such an event is similar to that of distant metastasis.

Most patients with high-grade primary bone sarcomas, unlike soft-tissue sarcomas, have distant micrometastases at presentation; an estimated 80% of patients with osteosarcomas have micrometastatic lung disease at the time of diagnosis. For that reason, in most

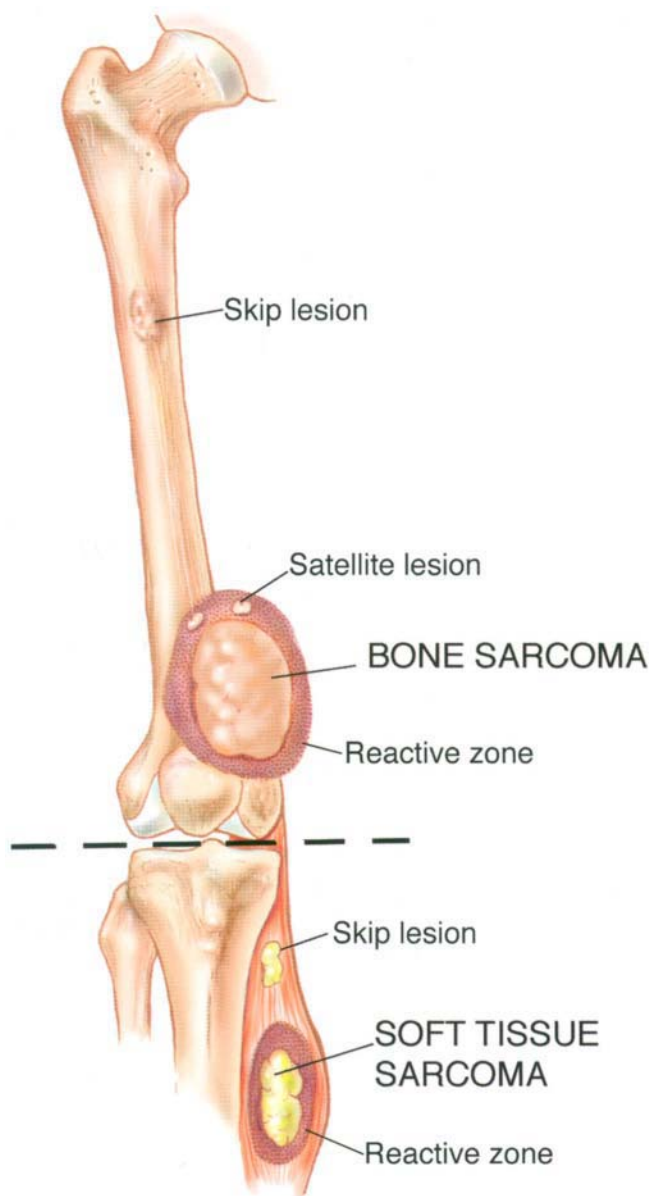


Figure 1.5 Biologic behavior of bone and soft-tissue sarcomas. Unique features are formation of reactive zone, intracompartmental growth, and, rarely, the presence of skip metastases. (Clin Orthop 1999 Nov; (368): 212–9)

cases, cure of a high-grade primary bone sarcoma can be achieved only with systemic chemotherapy and surgery. As mentioned, high-grade soft-tissue sarcomas have a smaller metastatic potential. Because of that difference in metastatic capability the role of chemotherapy in the treatment of soft-tissue sarcomas and its impact on survival are still a matter of controversy.

STAGING OF MUSCULOSKELETAL TUMORS

Staging is the process of classifying a tumor, especially a malignant tumor, with respect to its degree of differentiation, as well as its local and distant extent, in order to plan the treatment and estimate the prognosis. Staging allows the surgeon to determine the type and the extent of the operation that is necessary for a specific type of tumor in a particular anatomical location, as well as the indication for neoadjuvant treatment modalities. Staging of a musculoskeletal tumor is based on the findings of the physical examination and the results of imaging studies. Biopsy and histopathological evaluation are essential components of staging, but should always be the final step. The concept and practice of biopsy of musculoskeletal tumors are discussed in Chapter 2.

Plain radiographs remain the key imaging modality in the evaluation of bone tumors. Based on medical history, physical examination, and plain radiographs, accurate diagnosis of bone tumors can be made in more than 80% of cases. Because of the fine trabecular detail revealed by plain radiographs, bone lesions of the extremities can be detected at a very early stage; lesions of the spine and pelvis, by contrast, are not diagnosed until a large volume of bone has been destroyed. Once a bone lesion is found, computerized tomography (CT) is the imaging modality of choice to evaluate the extent of bone destruction. Magnetic resonance imaging (MRI) has been proven to be superior to CT in the evaluation of the intramedullary and extraosseous, extent of bone tumors (Figure 1.11).

In their early stages, soft-tissue tumors are hard to detect due to the lack of bone involvement. Occasionally, distortion of fat planes in plain radiographs implies the presence of a soft-tissue mass.

CT should be performed on a helical scanner that enables improved two-dimensional images and three-dimensional reconstruction capability. The field of view should be small enough to allow adequate resolution, particularly of the lesion and the adjacent neurovascular bundle and muscle groups. The slice thickness should be designed in order to allow at least 10–15 slices through the tumor. Intravenous contrast dye should be employed in the evaluation of soft-tissue tumors unless a clear contraindication for its use exists. On the other hand, contrast dye is of little value in the evaluation of bone tumors.

MRI is a valuable tool in the evaluation of soft-tissue tumors and of the medullary and soft-tissue components of bone tumors. The signal intensity of a tumor is assessed by comparing it with that of the adjacent soft tissues, specifically skeletal muscle and subcutaneous fat. MRI also enables one to view a lesion in all three planes (axial, sagittal, and coronal). Contrast-

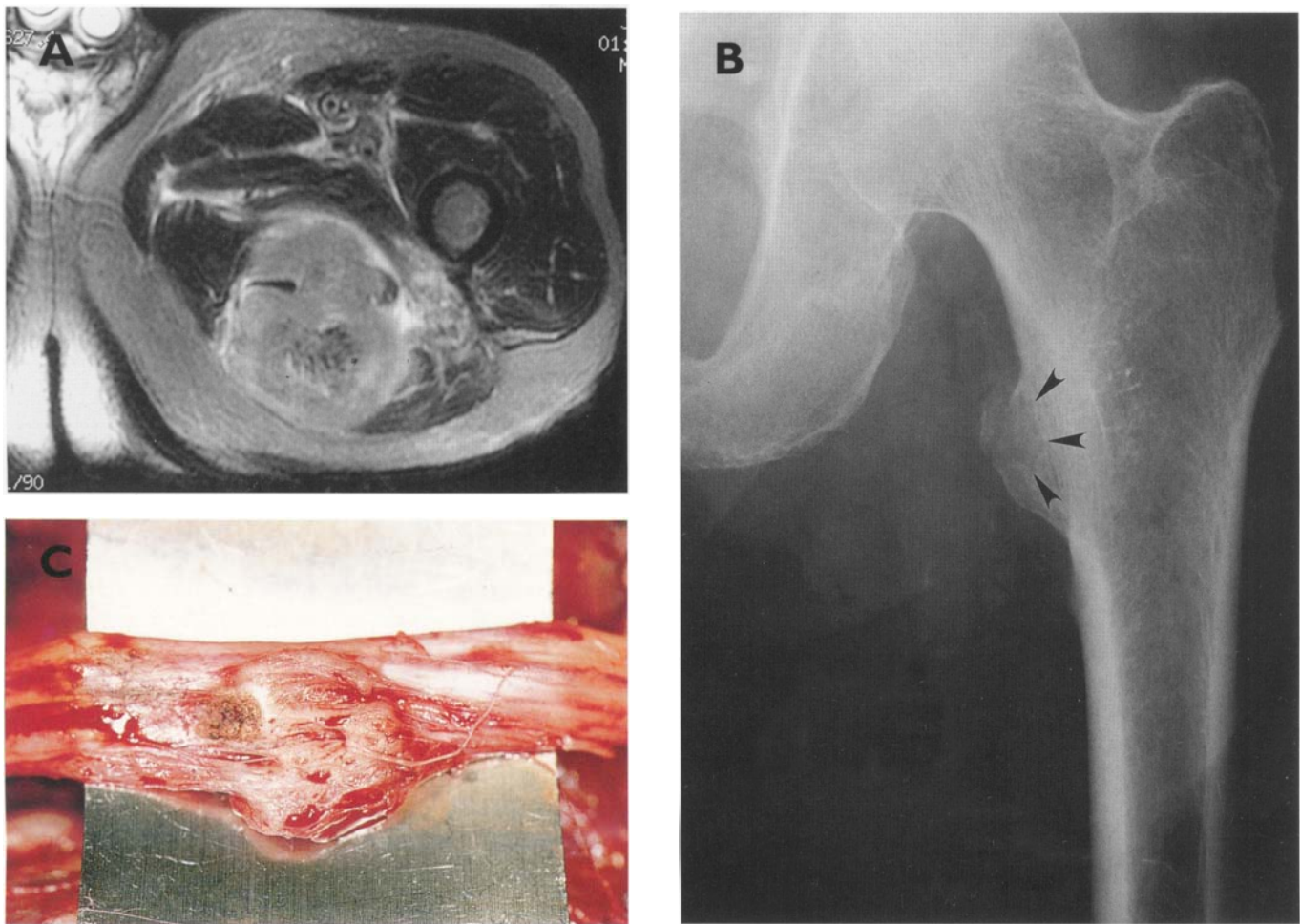


Figure 1.6 (A) Axial MRI, showing metastatic bladder carcinoma to the posterior thigh. (B) Plain radiograph of the proximal femur revealed direct invasion through the cortical bone with a pathological fracture of the lesser trochanter (arrows). (C) In surgery, exploration of the sciatic nerve revealed direct tumor involvement with extension under the epineurial sheath.

enhanced MRI is useful in evaluating the relationship of a tumor to the adjacent blood vessels and in characterizing cystic lesions. The presence of orthopedic hardware or surgical clips is not a contraindication to the performance of MRI; however, if a lesion is immediately adjacent to the location of the hardware, the local field may be distorted.

Although the purpose of MRI is to evaluate the anatomical extent of a lesion, it also can accurately diagnose a variety of soft-tissue tumors, including lipomas, liposarcomas, synovial cysts, pigmented villonodular synovitis, hemangiomas, and fibromatoses. Hematomas frequently have a characteristic appearance in MRI; however, high-grade sarcomas that have undergone significant intratumoral hemorrhage may resemble hematomas. For this reason the diagnosis of a simple hematoma should be made cautiously and, once it is made, close clinical monitoring must be made until the condition has been resolved. The general guidelines

regarding narrowing of the field and recommended number of slices per tumor are similar to those of CT.

Bone scintigraphy was traditionally used to assess the medullary extension of a primary bone sarcoma. As a rule the bone was cut approximately 6 cm proximal to the margin of the increased uptake. MRI allows more accurate determination of the medullary tumor extent; as a result, safer resections in narrower margins can be performed. Bone scan is currently used to determine the presence of metastatic and polystotic bone disease and the involvement of a bone by an adjacent soft-tissue sarcoma. In addition, the appearance of a bone lesion in the flow and pool phases of a three-phase bone scan reflects its biological activity and may be helpful in its diagnosis. It is also used as an indirect means of evaluating tumor response to chemotherapy.

Angiography is essential prior to surgery because vascular displacement is common in tumors that have a large extraosseous component. Blood vessels are likely



Figure 1.7 Pericapsular extension of an osteosarcoma of the proximal humerus (arrows).

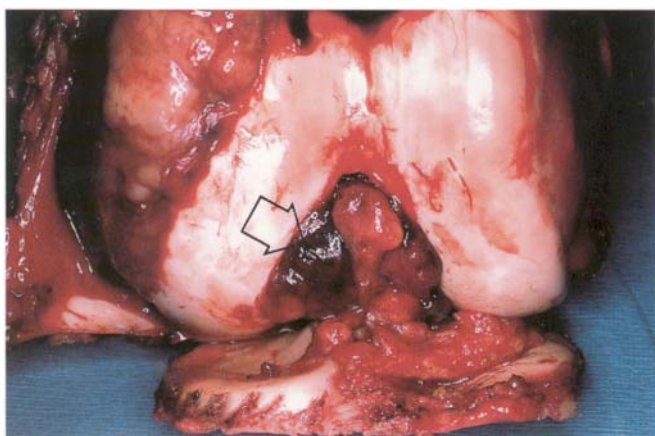


Figure 1.8 Extension of an osteosarcoma of the distal femur to the knee joint along the cruciate ligaments (arrow points to tumor); the articular cartilage is intact. Knee joint extension of a high-grade sarcoma of the distal femur is a rare event, necessitating extra-articular resection (i.e., en-bloc resection of the distal femur, knee joint, and a component of the proximal tibia), as shown in this figure.

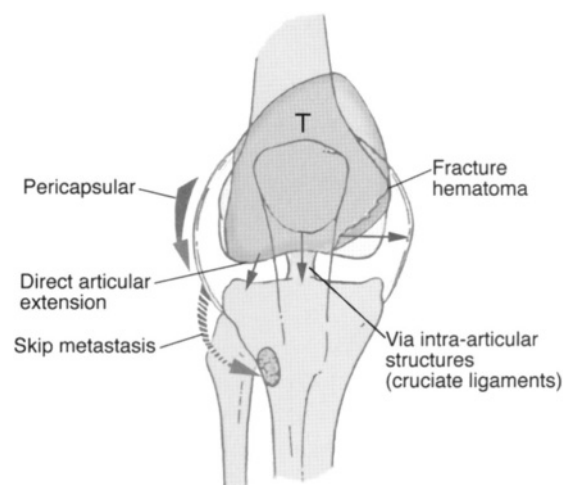


Figure 1.9 The five major mechanisms of joint involvement by a bone sarcoma. The most common mechanisms are pathologic fracture and pericapsular extension. (Cancer: Principles & Practice of Oncology, 6th Edition, 2001; 39.2: 1891–1935)

to be distorted or, less commonly, directly incorporated to the tumor mass. Angiography provides information that helps the surgeon plan the anatomical approach and gauge the likelihood that a major blood vessel has to be resected en-bloc with the tumor. It can also detect vascular anomalies (Figure 1.12) and establish patency of collateral vessels. Proximal femur resection, for example, frequently necessitates ligation of the profundus femoral artery (PFA). A patent superficial femoral artery (SFA) must be documented by angiography prior to surgery, otherwise the extremity will suffer severe ischemia following ligation of the PFA. Preoperative embolization may be useful in preparation for resection of metastatic vascular carcinomas if an intralesional procedure is anticipated. Metastatic hypernephroma is an extreme example of a vascular lesion that may bleed extensively and cause exsanguination upon the execution of an intralesional procedure without prior embolization.

Intra-arterial administration of chemotherapy allows the use of another type of information that can be obtained from angiographs; reduction in tumor vascularity. As revealed by serial angiographs, such reduction was shown to be indicative of good response to preoperative chemotherapy. Figure 1.13 summarizes the use of the various imaging modalities in the staging process of a primary bone sarcoma.

There is no single universally accepted staging system for soft-tissue and bone sarcomas. Some systems are valuable in the determination of the operative strategy, whereas others may be more useful in the estimation of the prognosis. An important variable in any staging system for musculoskeletal tumors, unlike a staging

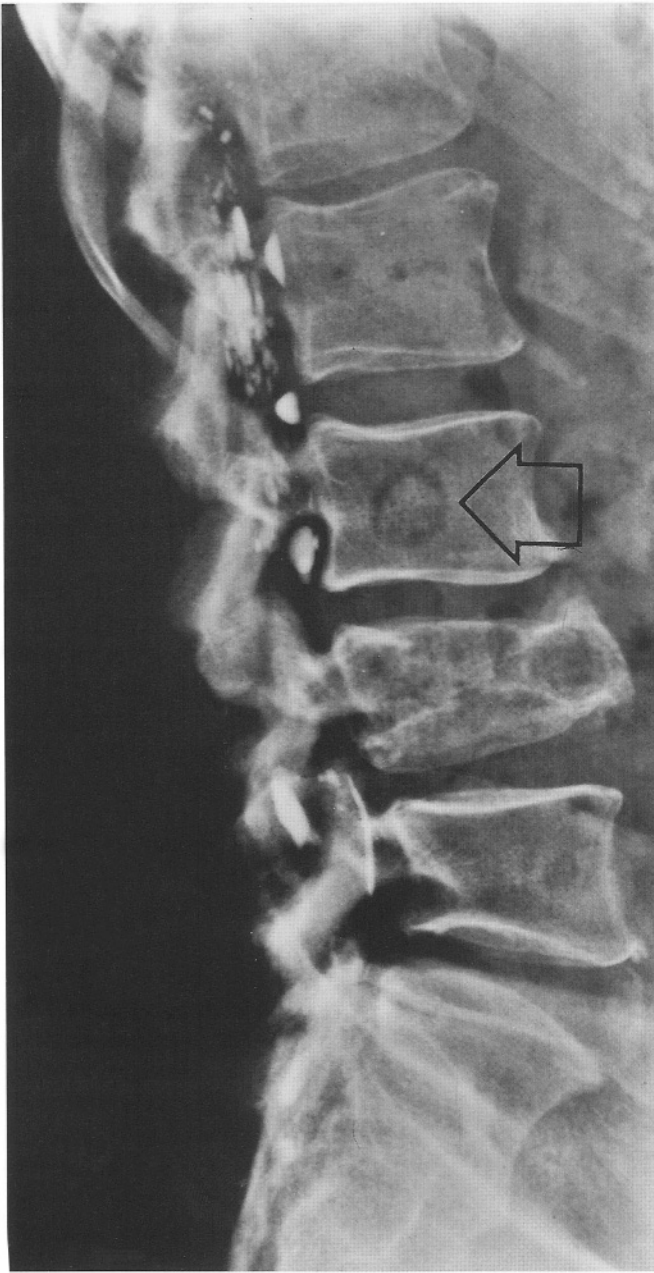


Figure 1.10 Lateral plain radiograph of the lumbar spine, showing metastatic high-grade osteosarcoma to the body of L3 vertebra (arrow).

system for carcinomas, is the grade of the tumor. The system that is most commonly used for the staging of **soft-tissue sarcomas** is that of the American Joint Committee on Cancer (Table 1.1).¹ It is based primarily on the Memorial–Sloan Kettering staging system and does not apply to rhabdomyosarcoma. Critics of this system point out that it is based largely on single-institution studies that were not subjected to multi-institutional tests of validity. The Musculoskeletal Tumor Society adopted staging systems that were

originally described by Enneking *et al.*,^{2,3} for malignant **soft-tissue** and **bone** tumors (Table 1.2), and the American Joint Committee on Cancer developed, with few changes, a staging system for malignant **bone** tumors (Table 1.3).⁴

Enneking's classical staging system is based on three factors: histological grade (G), site (T), and the presence or absence of metastases (M). The anatomical site (T) may be either intracompartmental (A) or extracompartmental (B). This information is obtained preoperatively on the basis of the data gained from the various imaging modalities. A tumor is classified as intracompartmental if it is bounded by natural barriers to extension, such as bone, fascia, synovial tissue, periosteum, or cartilage. An extracompartmental tumor may be either a tumor that violated the borders of the compartment from which it originated, or a tumor that originated and remained in the extracompartmental space. A tumor is assigned to stage III (M1) if a metastasis is present at a distant site or in a regional lymph node. It should be emphasized that Enneking's classification system is based on clinical data from an era in which chemotherapy was not given preoperatively and compartmental resections were much more common. Therefore, there was a clear correlation between the extent of the tumor at presentation, its relation to the boundaries of the compartment in which it is located, and the extent of surgery. A close correlation was also found between surgical stage of bone sarcoma and patient survival (Figure 1.14). Since that time the use of neoadjuvant chemotherapy was shown to decrease tumor size and facilitate limb-sparing surgery, as well as reduce the local recurrence rate. As a result, compartmental resections became rare. Nonetheless, Enneking's classification is based on the biological behavior of soft-tissue and bone sarcomas, and its underlying concept is as relevant as it was in the early 1980s.

Enneking also described a staging system of benign bone tumors, which remains the one that is most commonly used (Table 1.4).² That system is based on the biological behavior of these tumors as suggested by their clinical manifestation and radiological findings. Benign bone tumors grow in a centrifugal fashion, as do their malignant counterparts, and a rim of reactive bone is typically formed as a response of the host bone to the tumor. The extent of that reactive rim reflects the rate at which the tumor is growing; it is usually thick and well-defined around slowly growing tumors, and barely detectable around fast-growing, aggressive tumors.

Latent benign bone tumors are classified as stage 1. Such tumors are usually asymptomatic and are commonly discovered as an incidental radiographic finding. Their natural history is to grow slowly during





Figure 1.12 Extensive giant-cell tumor of the proximal tibia. Angiography was performed prior to a proximal tibia resection. It documented an absent peroneal artery. A successful effort was made to preserve the anterior tibial artery during the resection; otherwise, the leg would have been dependent on a single vessel.

normal growth of the individual and then to stop and, in most cases, heal spontaneously. These lesions never become malignant and usually heal following simple curettage. Examples include fibrous cortical defects and nonossifying fibromas (Figure 1.15). **Active benign** bone tumors are classified as stage 2 lesions. These tumors grow progressively but do not violate natural barriers. Associated symptoms may occur. Curettage and burr drilling are curative in most cases (Figure 1.16). **Aggressive** benign bone tumors (stage 3) may cause destruction of surrounding bone and usually break through the cortex into the surrounding soft tissues. Local control can be achieved only by curettage and meticulous burr drilling with a local adjuvant such as liquid nitrogen, or by resection of the lesion with a margin of normal tissue (i.e., wide resection) (Figure 1.17).

CLASSIFICATION OF SURGICAL PROCEDURES

There are four basic types of excisions; each is based on the relationship of the dissection plane to the tumor and its pseudocapsule. An **intralesional** excision is performed within the tumor mass and results in removal of only a portion of it; the pseudocapsule and macroscopic tumor are left behind. In a **marginal** excision, the dissection plane passes through the pseudocapsule of the tumor. Such a resection may leave microscopic disease. **Wide** (en-bloc) excision entails removal of the tumor, its pseudocapsule, and a cuff of normal tissue peripheral to the tumor in all directions. This is the desired margin for sarcoma resection; however, the adequate thickness of the normal tissue cuff is a matter of controversy. For both soft-tissue and

Table 1.1 System of the American Joint Committee on Cancer for the staging of soft-tissue sarcomas¹

Stage ^a	Grade ^b	Primary tumor ^c	Metastasis in regional lymph nodes ^d	Distant metastasis ^e
IA	G ₁ or G ₂	T _{1a} or T _{1b}	N ₀	M ₀
IB	G ₁ or G ₂	T _{2a}	N ₀	M ₀
IIA	G ₁ or G ₂	T _{2b}	N ₀	M ₀
IIB	G ₃ or G ₄	T _{1a} or T _{1b}	N ₀	M ₀
IIC	G ₃ or G ₄	T _{2a}	N ₀	M ₀
III	G ₃ or G ₄	T _{2b}	N ₀	M ₀
IV	Any G	Any T	N ₀ or N ₁	M ₁

^aIA = Low-grade, small, and superficial or deep; IB = low-grade, large, and superficial; IIA = low-grade, large and deep; IIB = high-grade, small, and superficial or deep; IIC = high grade, large, and superficial; III = high-grade, large, and deep; IV = any with metastasis.

^bG₁ = Well differentiated; G₂ = moderately well differentiated; G₃ = poorly differentiated; G₄ = undifferentiated.

^cT₁ = Tumor is ≤ 5 cm in greatest dimension; T_{1a} = T₁ tumor is superficial (lesion does not involve the superficial fascia); T_{1b} = T₁ tumor is deep (lesion is deep to or invades the superficial fascia; that is, all intraperitoneal visceral lesions or lesions that invade major vessels or that are located in the thorax, head, or neck); T₂ = tumor that is > 5 cm in greatest dimension; T_{2a} = T₂ tumor is superficial; T_{2b} = T₂ tumor is deep.

^dN₀ = No metastasis in regional lymph nodes; N₁ = metastasis in regional lymph nodes.

^eM₀ = No distant metastasis; M₁ = distant metastasis.

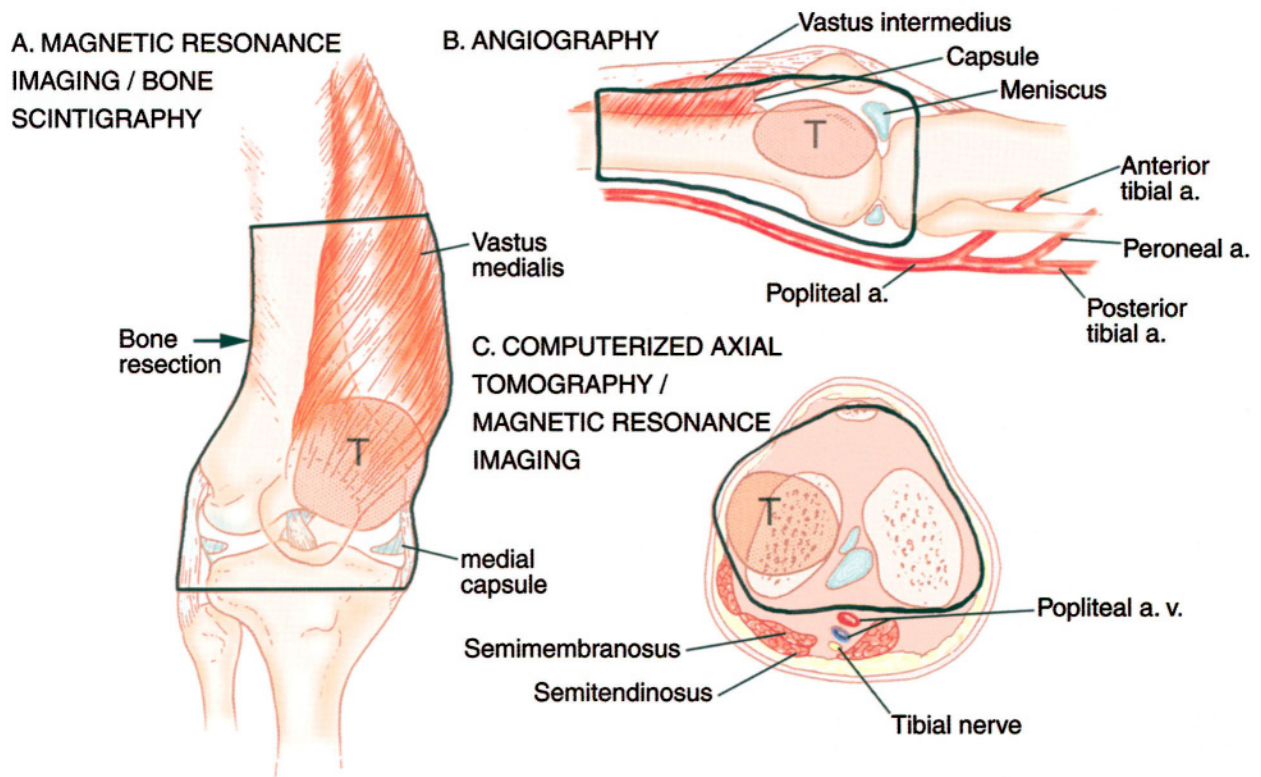


Figure 1.13 Relationship of the various imaging modalities to the different components of a bone sarcoma. Plain radiographs assess bony involvement and cortical breakdown. CT determines the exact extent of bone destruction and MRI determines the medullary and extraosseous components of the tumor. Bone scan evaluates the cortical and intraosseous extents of the tumor, as well as the presence of metastatic bone disease. Angiography reveals the anatomic relation of the tumor to the major blood vessels. (Cancer: Principles & Practice of Oncology. 5th Edition, 1997; 38.3:1789–1852)

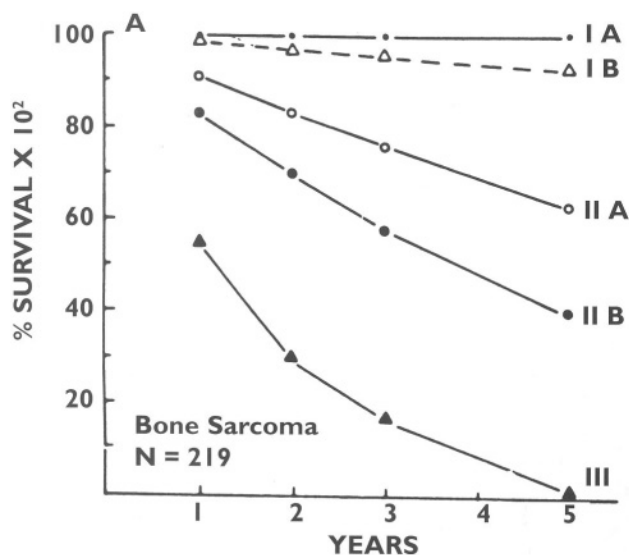


Figure 1.44 Survival by Enneking's surgical stage of 219 patients with primary bone sarcoma. (Cancer: Principles & Practice of Oncology. 5th Edition, 1997; 38.3: 1789–1852)

Table 1.2 System of Enneking *et al.*^{2,3} for staging of soft-tissue and bone sarcomas

Stage	Grade ^a	Site ^b	Metastasis ^c
IA	G ₁	T ₁	M ₀
IB	G ₁	T ₂	M ₀
IIA	G ₂	T ₁	M ₀
IIB	G ₂	T ₂	M ₀
III	G ₁ or G ₂	T ₁ or T ₂	M ₁

^aG₁ = Low grade; G₂ = high grade.

^bT₁ = Intracompartmental; T₂ = extracompartmental.

^cM₀ = No regional or distant metastasis; M₁ = regional or distal metastasis. (Cancer: Principles & Practice of Oncology. 6th Edition, 2001; 39.2: 1891–1935)

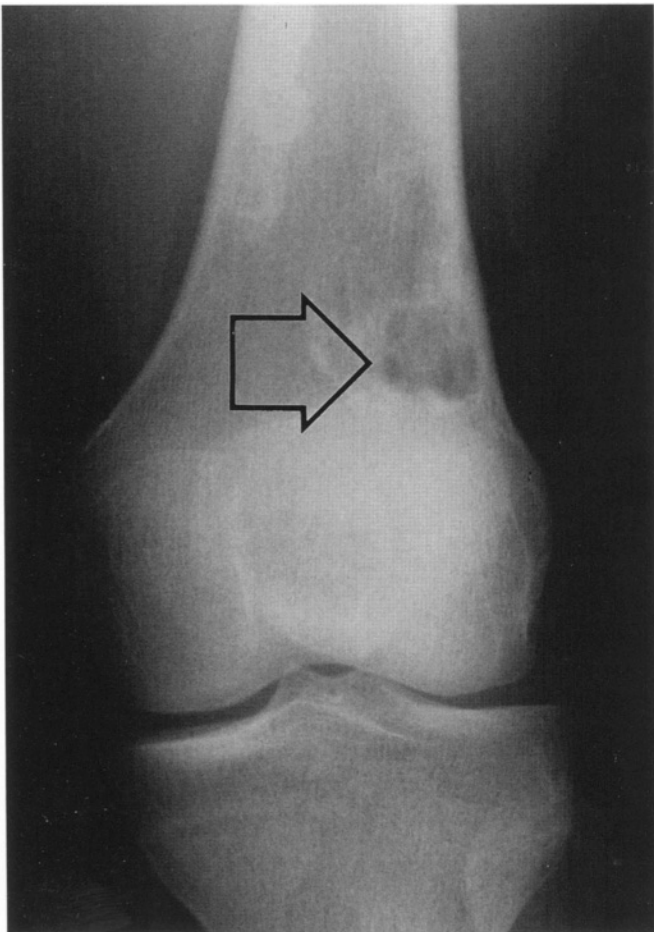


Figure 1.15 Nonossifying fibroma (NOF) of the distal femur (arrow). As in most cases of NOF, the lesion was asymptomatic and the plain radiographs were ordered because of a trauma to the knee.



Figure 1.16 (see above right and bottom right) Aneurysmal bone cyst of the distal tibia as seen by plain radiographs, (A) anteroposterior and (B) lateral views.

Table 1.3 System of the American Joint Committee on Cancer for the staging of sarcomas of bone⁴

Stage	Grade ^a	Primary tumor ^b	Metastasis in regional lymph nodes ^c	Distant metastasis ^d
IA	G ₁ or G ₂	T ₁	N ₀	M ₀
IB	G ₁ or G ₂	T ₂	N ₀	M ₀
IIA	G ₃ or G ₄	T ₁	N ₀	M ₀
IIB	G ₃ or G ₄	T ₂	N ₀	M ₀
III	Not defined			
IVA	Any G	Any T	N ₁	M ₀
IVB	Any G	Any T	Any N	M ₁

^aG₁ = Well differentiated; G₂ = moderately differentiated; G₃ = poorly differentiated; G₄ = undifferentiated.

Ewing's sarcoma and malignant lymphoma are graded as G₄.

^bT₁ = Tumor confined within the cortex; T₂ = tumor extends beyond the cortex.

^cN₀ = No metastasis in regional lymph nodes; N₁ = metastasis in regional lymph nodes.

^dM₀ = No distant metastasis; M₁ = distant metastasis.

Table 1.4 Enneking's system for the staging of benign bone tumors²

Stage	Definition	Biological behavior	Typical example	
			Soft-tissue tumor	Bone tumor
1	Latent	Remains static or heals spontaneously	Lipoma	Nonossifying fibroma
2	Active	Progressive growth, limited by natural barriers	Angiolipoma	Aneurysmal bone cyst
3	Aggressive	Progressive growth, invasive, not limited by natural barriers	Aggressive fibromatosis	Giant-cell tumor



Figure 1.17 Plain radiographs, (A) anteroposterior and (B) lateral views of benign giant-cell tumor of the proximal tibia. The tumor was neglected for 18 months and necessitated proximal tibia resection and reconstruction with endoprosthesis.

bone sarcomas, it is generally believed to be a few centimeters.

Radical excision involves removal of the tumor and the entire anatomical compartment within which it is located (Figures 1.18, 1.19). Although traditionally mentioned as the fourth excision type, it does not define the component of the tumor that is left behind. In other words, a radical excision can achieve a marginal or a wide margin, depending on how close the tumor is to the border of the compartment. However, radical excision excludes the possibility of skip metastases.

In general, benign bone tumors are adequately treated by either an intralesional procedure (curettage and burr drilling, cryosurgery) or by marginal excision. Primary bone sarcomas are treated with wide excision. Metastatic tumors are treated according to the general intent of the surgery. When a palliative surgery is performed, metastatic lesions are treated by an

intralesional procedure. If a curative procedure is performed, as in the case of solitary breast metastasis, for example, the lesion is treated as if it was a primary bone sarcoma (i.e., wide excision). It is important to emphasize that any of these excision types may be accomplished by a limb-sparing procedure or by amputation. An amputation is *not* necessarily an adequate cancer operation, but it is a method of achieving a specific margin. It may entail a marginal, wide, or radical excision, depending upon the plane in which it passes. Staging studies are used to assess local tumor extent and relevant local anatomy, and thereby determine how a desired surgical margin may be achieved.

SOFT-TISSUE SARCOMAS

Soft-tissue sarcomas are a heterogeneous group of rare tumors that arise from the supporting extraskeletal

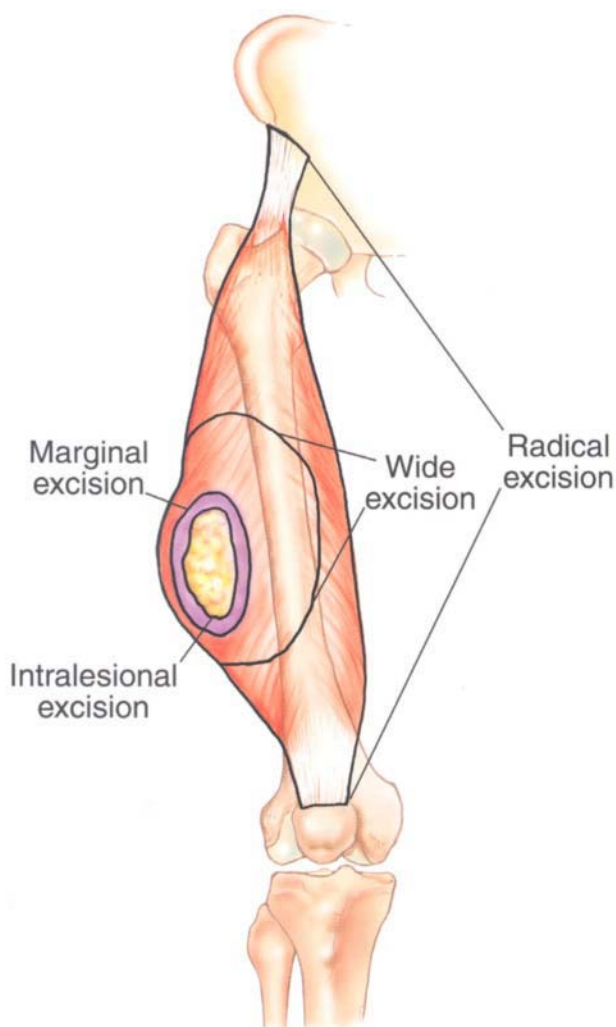


Figure 1.18 Various excision types for soft-tissue sarcoma.

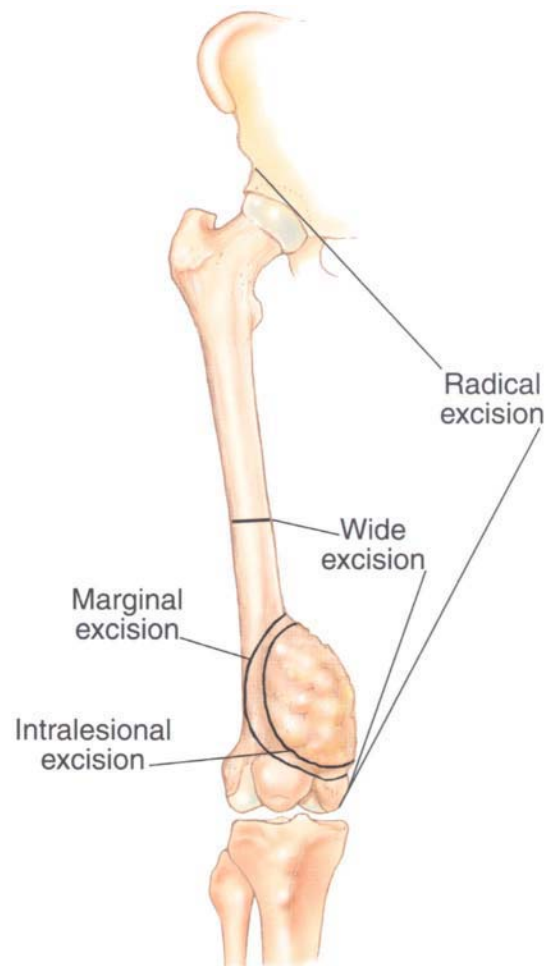


Figure 1.19 Various excision types for bone sarcoma.

tissues (i.e., muscle, fascia, nerve, connective, fibrous, and fatty tissues). Although they share biological characteristics, and are treated in a similar fashion, each of the various soft-tissue sarcomas has a unique morphology, biological behavior, and prognosis. Pathologic grading is at times difficult. In general, the extent of pleomorphism, atypia, mitosis, and necrosis correlates with the grade of malignancy. Notable exceptions are synovial sarcomas, which tend to behave like high-grade lesions even in the absence of histopathological high-grade characteristics. The exact histogenesis often cannot be accurately defined, although the grade can be determined.

Pathologic Characteristics of Specific Soft-tissue Sarcomas

Malignant Fibrous Histiocytoma

Malignant fibrous histiocytoma (MFH) is the most common soft-tissue sarcoma in adults. It most commonly affects the lower extremity and has a predilection for originating in deep-seated skeletal muscles. The tumor usually presents as a multinodular mass with well-circumscribed or ill-defined infiltrative borders. The size at the time of diagnosis often correlates with the ease of clinical detection: superficial variants, presenting as dermal or subcutaneous masses, may be only a few centimeters in diameter, whereas those arising in the retroperitoneum often attain a diameter of 15 cm or greater. Color and consistency vary considerably and reflect, in part, the cellular composition. Red-brown areas of hemorrhage and necrosis are not uncommon (Figure 1.20).

The myxoid variant of MFH contains a predominance of white-gray, soft, mucoid tumor lobules, created by the high content of myxoid ground substance. Approximately 5% of MFHs undergo extensive hemorrhagic cystification, often leading to a clinical and radiologic diagnosis of hematoma. A needle biopsy can result in a benign diagnosis if only the hemorrhagic center of the tumor is sampled. For these reasons, until proven otherwise, one should assume that an underlying soft-tissue sarcoma is present in any adult patient with a deep-seated hematoma that does not resolve after a few weeks, even when there is a history of trauma to that site.

The currently accepted broad histologic spectrum of MFH encompasses many variants that were formerly considered to be distinct clinicopathologic entities. These lesions, which had been named according to the predominant cell type, include fibroxanthoma, malignant fibroxanthoma, inflammatory fibrous histiocytoma, and giant cell tumor of soft part. Immunohistochemical studies and electron microscopy

can assist in the accurate diagnosis of a significant percentage of these tumors. The basic neoplastic cellular constituents of all fibrohistiocytic tumors include fibroblasts, histiocyte-like cells, and primitive mesenchymal cells (Figure 1.21). In addition, there is usually an acute and a chronic inflammatory cell component. The proportion of these malignant and reactive cell elements, the degree of pleomorphism of the neoplastic cells, and the predominant pattern accounts for the wide histologic variances.

The most common histologic pattern associated with MFH is a storiform arrangement of the tumor cells. This is characterized by fascicles of spindle cells that

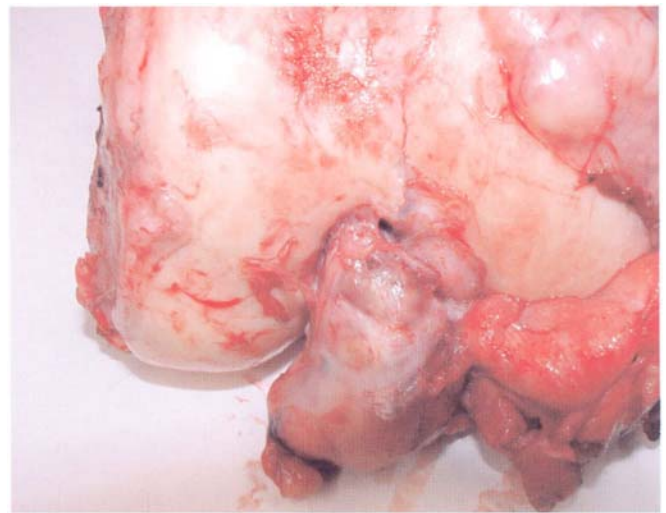


Figure 1.20 Deep-seated malignant fibrous histiocytoma (MFH) presents as a soft, white-tan mass, often with areas of hemorrhage and necrosis. Occasionally, cysts and hematoma-like changes are present.

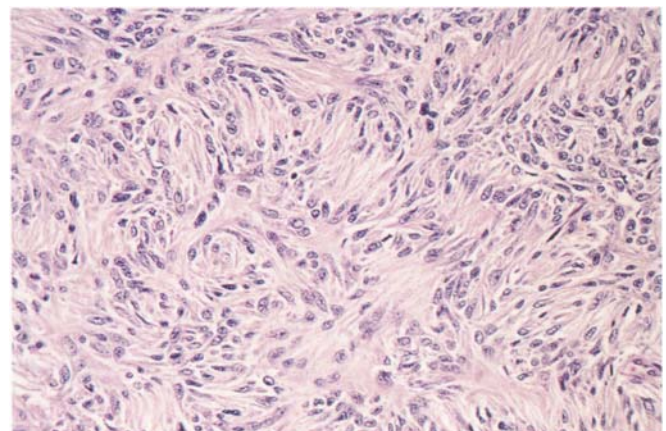


Figure 1.21 MFH, a high-grade sarcoma, is characterized by pleomorphic spindle cells forming fascicular or typical storiform patterns. Bizarre tumor giant cells are interspersed throughout the mass. Atypical mitotic figures are frequently seen.

intersect to form a pinwheel or cartwheel pattern (Figure 1.21). Atypical and bizarre giant cells, often containing abnormal mitotic figures, may occur. The histologic grade (almost always intermediate to high) is a good prognosticator of metastatic disease. In the myxoid variant, the second most common histologic type, the tumor cells are dispersed in a richly myxoid matrix (Figure 1.22). The less common giant cell type (malignant giant cell tumor of soft parts) is characterized by abundant osteoclast-like giant cells that are diffusely distributed among the malignant fibrohistiocytic elements. Myxoid MFH has a more favorable prognosis than other subtypes.

Liposarcoma

Liposarcoma is the second most common soft-tissue sarcoma in adults. It has a wide range of malignant potential that correlates well with the histologic classification of the individual tumor. The lower extremity is the most common site and accounts for greater than 40% of the cases. These tumors, particularly those arising in the retroperitoneum, can attain enormous size; specimens measuring 10–15 cm and weighing greater than 5 kg are not uncommon (Figure 1.23). Liposarcomas tend to be well circumscribed and multilobulated. Gross features usually correlate with the histologic composition. Well-differentiated liposarcomas contain variable proportions of relatively mature fat and fibrocollagenous tissues, vary from yellow to white–gray and can be soft, firm, or rubbery. A tumor that is soft, pink–tan, and reveals a mucinous surface is

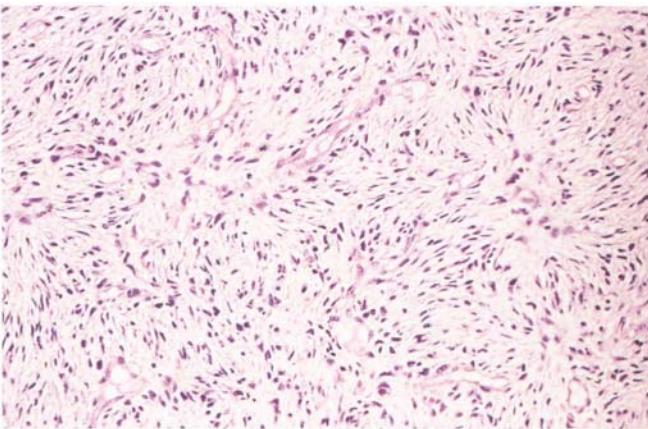


Figure 1.22 The myxoid variant of MFH discloses copious mucinous-like interstitial substance that consists predominantly of hyaluronic acid. The cellular components can be widely dispersed, imparting a deceptively bland appearance, particularly on a needle-biopsy specimen. Thorough sampling of the tumor usually discloses more diagnostic features.

probably a myxoid liposarcoma, which is the most common histologic type. The high-grade liposarcomas (round cell and pleomorphic) vary from pink–tan to brown and may disclose extensive hemorrhage and necrosis.

Identification of typical lipoblasts is mandatory to establish the diagnosis of liposarcoma. This diagnostic cell contains one or more round, cytoplasmic fat droplets that form sharp, scalloped indentations on the central or peripheral nucleus. Well-differentiated liposarcomas often contain a predominance of mature fat cells and only a few, widely scattered lipoblasts. Inadequate sampling can therefore lead to a misdiagnosis of a benign lipoma (Figure 1.24). Well-differentiated liposarcomas that arise in the superficial soft tissues have been called “atypical lipomas.” In the sclerosing variant of a well-differentiated liposarcoma, delicate collagen fibrils that encircle fat cells and lipoblasts comprise a prominent part of the matrix



Figure 1.23 Large, low-grade liposarcoma of the posterior thigh.

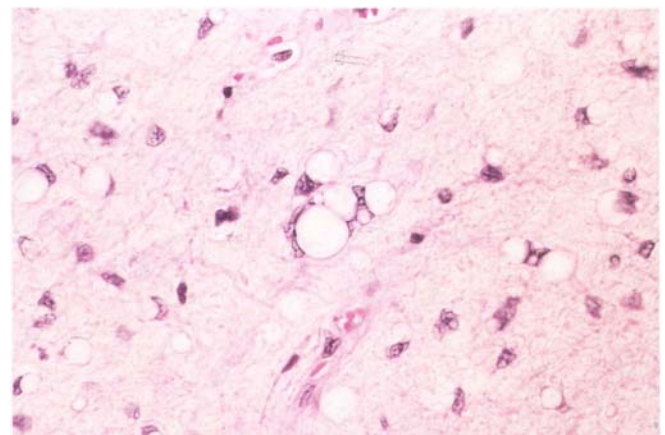


Figure 1.24 The diagnosis of a well-differentiated liposarcoma depends on the identification of characteristic lipoblasts. These cells can be mono- or multivacuolated with hyperchromatic, scalloped nuclei. This variant can closely mimic ordinary lipoma.

(Figure 1.25). In rare cases, well-differentiated liposarcomas, usually after multiple local recurrences, transform into a high-grade spindle-cell sarcoma, often with MFH-like features ("dedifferentiated liposarcoma"). This change imparts a high risk of metastases.

A diagnosis of myxoid liposarcoma requires the observation of a delicate plexiform capillary network associated with both primitive mesenchyme-like cells and a variable number of lipoblasts (Figure 1.26). The stroma contains a high proportion of myxoid ground substance that may form numerous microcysts. In round-cell liposarcomas, the lipoblasts are interspersed within sheets of poorly differentiated round cells (Figure 1.27). There is convincing evidence that myxoid and round-cell liposarcomas are the divergent ends of a continuous spectrum of the same neoplasm. This is supported by the fact that both tumors have the same

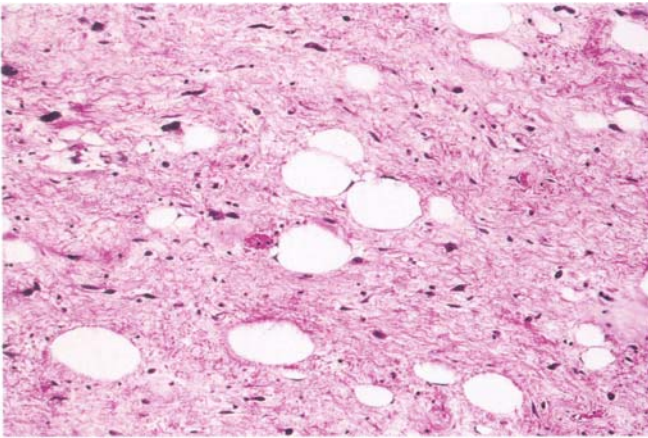


Figure 1.25 The sclerosing variant of well-differentiated liposarcoma contains a background of coarse wavy collagen fibers. The lipoblasts are dispersed among these fibers.

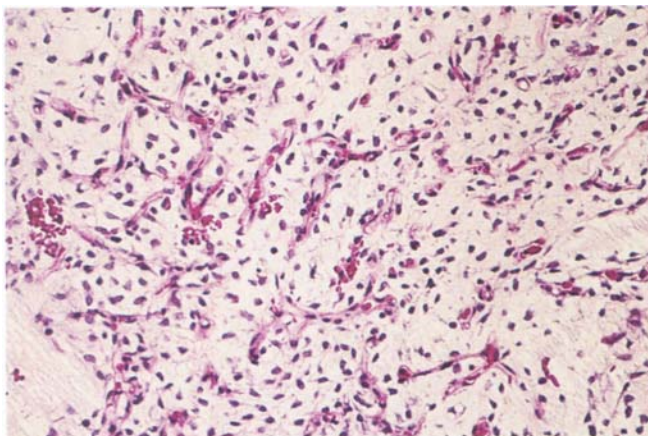


Figure 1.26 Lipoblasts associated with a plexiform capillary network in a diffusely myxoid stroma define the myxoid liposarcoma. Cyst-like areas are occasionally present.

chromosomal translocation. Finally, pleomorphic liposarcoma discloses a mixture of bizarre, often multivacuolated, lipoblasts and atypical stromal cells, many of which contain abnormal mitotic figures (Figure 1.28). Areas of necrosis and hemorrhage are common. The presence of lipoblasts distinguishes this high-grade sarcoma from MFH and other pleomorphic sarcomas.

Unlike other soft-tissue sarcomas, liposarcomas may be multiple and occur in unusual sites in the same individual. Therefore, careful evaluation of other masses in a patient with a liposarcoma is mandatory. Accurate determination of the morphologic subtype and its grade is essential. Low-grade liposarcomas are

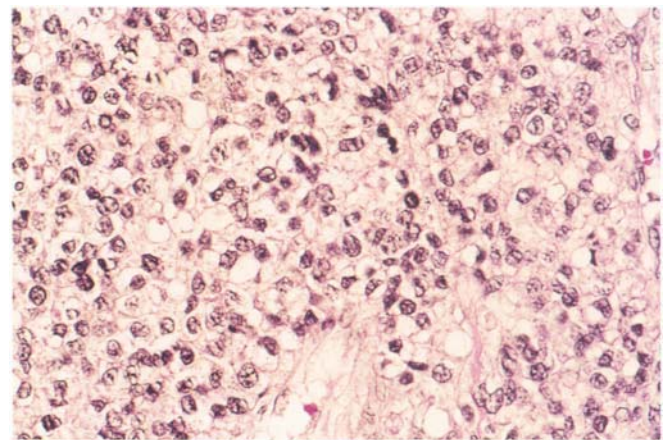


Figure 1.27 Sheets of round blue cells with clear to eosinophilic cytoplasm are typical of round-cell liposarcoma, a high-grade neoplasm. It has the identical chromosomal abnormality found in myxoid liposarcoma, evidence that these are morphologic variants of the same tumor.

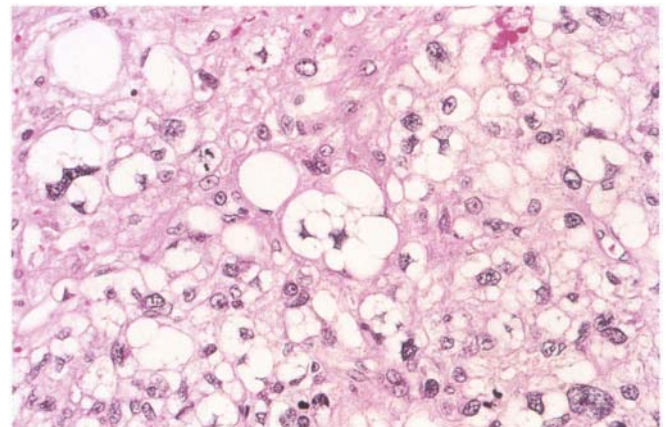


Figure 1.28 The pleomorphic liposarcoma is another high-grade form of lipomatous malignancy. It is characterized by numerous large, bizarre lipoblasts, abnormal mitotic figures, and necrosis. Many of its features overlap with malignant fibrous histiocytoma.

treated with wide excision and adjuvant radiation therapy is recommended only if marginal margins were achieved. The authors treat high-grade liposarcomas as any other high-grade soft-tissue sarcoma; neoadjuvant chemotherapy, wide excision, and adjuvant chemotherapy. Radiation therapy is indicated if wide margins were not achieved. The role of chemotherapy and radiation therapy in the treatment of soft tissue is discussed in Chapters 3 and 5, respectively.

Fibrosarcoma

Fibrosarcoma used to be considered the most common soft-tissue sarcoma. Following the histopathologic definition of MFH as a distinct entity and the subsequent assignment of "pleomorphic fibrosarcoma" to that category, fibrosarcoma has become uncommon. Fibrosarcomas usually arise from the fascial and aponeurotic structures of the deep soft tissues. Superficial variants are rare. Relatively small tumors present as firm, gray–white, partially to completely circumscribed masses (Figure 1.29). As these lesions enlarge, a more diffusely infiltrative pattern predominates.

The fundamental cell of this neoplasm is the fibroblast, which is a spindle cell capable of producing collagen fibers. The collagen matrix, appearing as birefringent wavy fibers, can be easily recognized in the more differentiated fibrosarcomas (Figure 1.30). Its presence can be confirmed with the application of Masson trichrome stain. Well-differentiated fibrosarcoma is characterized by intersecting fascicles of relatively uniform spindle cells showing minimal atypical features and sparse mitotic figures. The fascicles often intersect at acute angles to form the typical herringbone pattern. Differentiating low-grade

fibrosarcomas from fibromatosis and its variants may be difficult. In contrast, poorly differentiated fibrosarcoma reveals a barely discernible fascicular arrangement. The smaller cells show significant pleomorphism, nuclear atypia, and often have a high mitotic rate. Necrosis and hemorrhage commonly occur in high-grade fibrosarcomas. In this situation, particularly in the presence of pleomorphic tumor cells, distinguishing fibrosarcoma from MFH is exceedingly difficult.

Synovial Sarcoma

Synovial sarcoma ranks as the fourth most common soft-tissue sarcoma. In spite of its name, this tumor rarely arises directly from a joint but rather arises in proximity to it with a propensity for the distal portion of the extremities. Synovial sarcomas occur in a younger age group than do most other sarcomas: most patients are below the age of 40. The tumor typically presents as a deep-seated, well-circumscribed, multinodular, firm mass. Contiguity with a synovium-lined space is rare and, occasionally, lymphatic spread occurs. Unlike most soft-tissue sarcomas, synovial sarcomas may be present as a painless mass for a few years. Plain radiographs often show small calcifications within the mass. That finding should alert the physician to the diagnosis.

Virtually all synovial sarcomas are high-grade. The poorly differentiated neoplasms usually present as ill-defined, infiltrative lesions with a soft, somewhat gelatinous consistency. The classic histologic presentation of this tumor is a biphasic pattern. This implies the presence of coexisting but distinct cell populations, namely, spindle cells and epithelioid cells (Figure 1.31).



Figure 1.29 The gross appearance of a well-differentiated fibrosarcoma is that of a white–gray whorled nodules. It has a firm rubbery consistency.

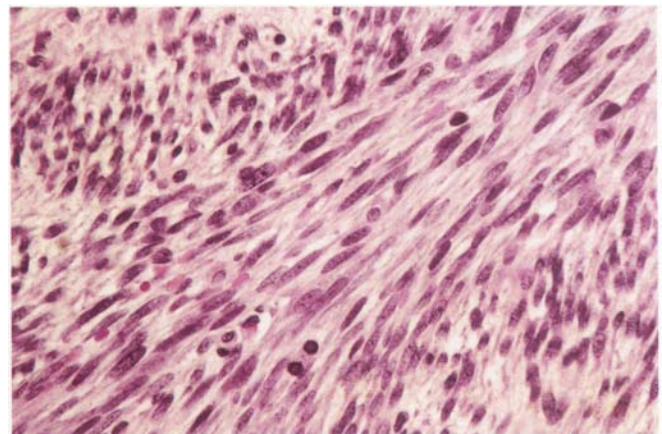


Figure 1.30 Low-grade fibrosarcoma is composed of slender, relatively uniform spindle cells forming elongated fascicles. These nodules often intersect at acute angles forming the typical herringbone pattern.

The plump spindle cells, usually the predominant component, form an interlacing fascicular pattern that is reminiscent of fibrosarcoma. Within the spindle-cell portion of the tumor, areas resembling the acutely branching vascular pattern of hemangiopericytoma are common. The arrangement of epithelioid cells varies from merely solid nests to distinct, gland-like structures (Figure 1.32). When comprising glandular spaces the constituent cells range from cuboidal to tall columnar; rarely do they undergo squamous metaplasia. The application of histochemical stains demonstrates that the glandular lamina contain epithelial-type acid mucins. The neoplasm may contain extensive areas of dense stromal hyalinization, and focal calcification is common. The presence of extensive areas of calcification, sometimes with modulation to benign osteoid, deserves recognition because this rare variant imparts a significantly more favorable prognosis than other forms of synovial sarcoma. The existence of a monophasic spindle cell synovial sarcoma has been recognized, although distinguishing it from fibrosarcoma can be difficult. In contrast to fibrosarcoma, the spindle cell variant of synovial sarcoma may contain cytokeratins, as demonstrated with immunohistochemical studies.

PATHOLOGIC CHARACTERISTICS OF SPECIFIC PRIMARY BONE SARCOMAS

Osteosarcoma

Osteosarcoma is the most common primary bone sarcoma. Its distinguishing characteristic is the production of "tumor" osteoid or immature bone matrix. Osteosarcoma typically occurs during childhood and

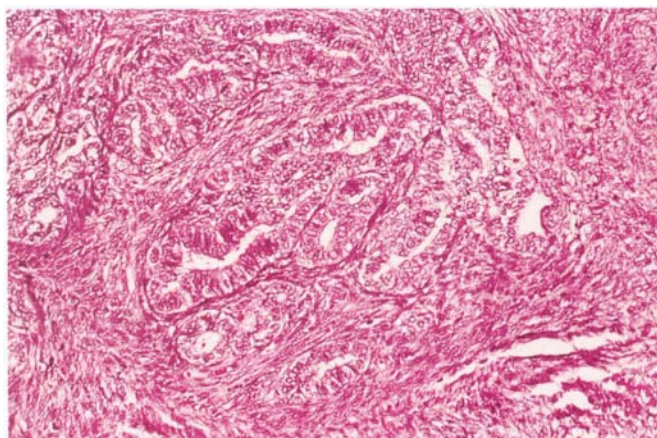


Figure 1.31 Synovial sarcoma is characterized by a distinctive biphasic pattern. This implies an admixture of spindle-cell areas along with epithelioid cells forming gland-like structures. The proportion of these two components is variable.

adolescence. In patients over the age of 40 it is usually associated with a pre-existent condition such as Paget's disease or irradiated bone. Between 80% and 90% of the tumors occur in the metaphysis of long bone with the most common sites being the distal femur, proximal tibia, and proximal humerus. Pain, accompanied by a tender, soft tissue swelling, is the most common complaint.

The classical radiologic appearance is a destructive tumor with increased intramedullary radiodensity, an area of radiolucency, and a pattern of permeative invasion of the surrounding bone with poorly defined borders, cortical destruction, periosteal elevation, extra-osseous extension, and soft-tissue calcification. On the basis of radiological presentation, osteosarcomas are classified into three broad categories: sclerotic osteosarcomas (30%), osteolytic osteosarcomas (25%), and mixed pattern (45%) (Figure 1.33). The differential diagnosis of this tumor includes giant-cell tumor, aneurysmal bone cyst, fibrosarcoma, and MFH of bone. Errors in diagnosis most often occur with pure osteolytic Osteosarcoma.

As the neoplasm permeates the cortex, the periosteum may be elevated. This stimulates reactive bone formation and accounts for a distinctive radiologic feature called "Codman's triangle". Longitudinal sectioning of the involved bone often reveals wide extension within the marrow cavity. Rarely, skip areas within the medullary canal can be demonstrated. There may be necrotic and hemorrhagic foci. At the time of diagnosis, most tumors have already caused substantial cortical destruction. Continued tumor growth results in involvement of the adjacent soft tissues (Figure 1.34).

The definitive diagnosis of osteosarcoma rests on the identification of a malignant stroma that produces an osteoid matrix. The stroma consists of a haphazard

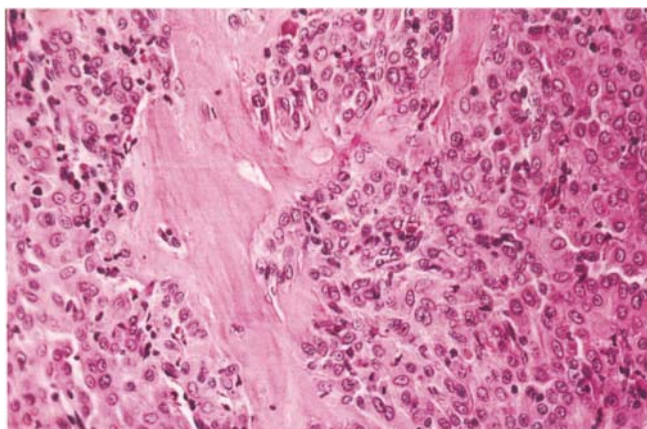


Figure 1.32 When only one of the elements of synovial sarcoma is present, almost invariably the spindle-cell component, it is termed monophasic synovial sarcoma.

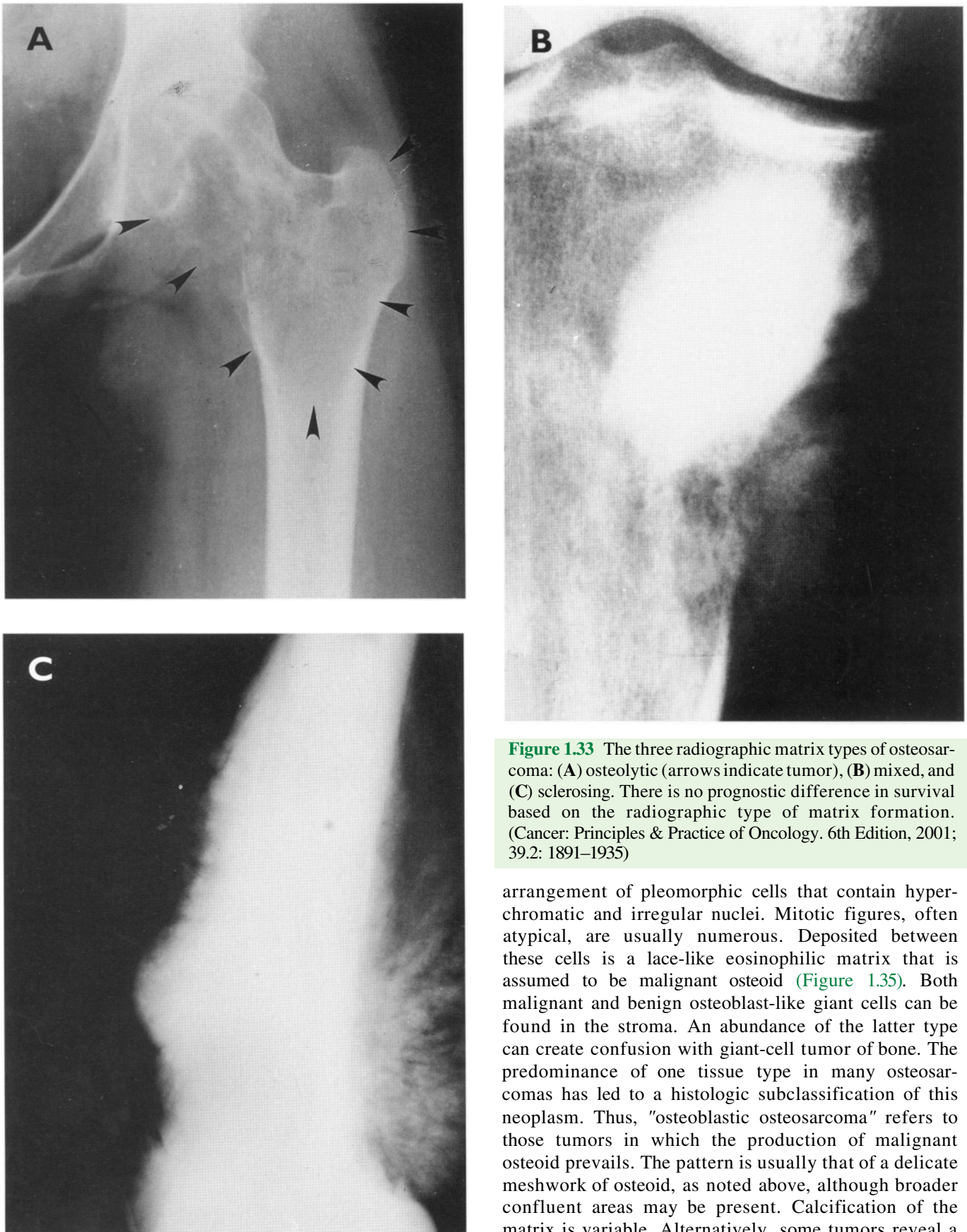


Figure 1.33 The three radiographic matrix types of osteosarcoma: (A) osteolytic (arrows indicate tumor), (B) mixed, and (C) sclerosing. There is no prognostic difference in survival based on the radiographic type of matrix formation. (Cancer: Principles & Practice of Oncology, 6th Edition, 2001; 39.2: 1891–1935)

arrangement of pleomorphic cells that contain hyperchromatic and irregular nuclei. Mitotic figures, often atypical, are usually numerous. Deposited between these cells is a lace-like eosinophilic matrix that is assumed to be malignant osteoid (Figure 1.35). Both malignant and benign osteoblast-like giant cells can be found in the stroma. An abundance of the latter type can create confusion with giant-cell tumor of bone. The predominance of one tissue type in many osteosarcomas has led to a histologic subclassification of this neoplasm. Thus, "osteoblastic osteosarcoma" refers to those tumors in which the production of malignant osteoid prevails. The pattern is usually that of a delicate meshwork of osteoid, as noted above, although broader confluent areas may be present. Calcification of the matrix is variable. Alternatively, some tumors reveal a

predominance of malignant cartilage production; hence, the term "chondroblastic osteosarcoma". Even though the malignant cartilaginous elements may be overwhelming, the presence of a malignant osteoid matrix warrants the diagnosis of osteosarcoma. Another variant, fibroblastic osteosarcoma, is characterized by large areas of proliferating fibroblasts arranged in intersecting fascicles. Such areas are indistinguishable from fibrosarcomas, and thorough sampling may be necessary to identify the malignant osteoid component. The so-called telangiectatic osteosarcoma contains multiple blood-filled cystic and sinusoidal spaces of variable size. Identification of marked cytologic atypia in the septae and more solid areas rules out the diagnosis of aneurysmal bone cyst.



Figure 1.34 High-grade osteosarcoma of the proximal humerus with cortical breakthrough and tumor extension into the soft tissues.

Variants of Osteosarcoma

There are 11 recognizable variants of osteosarcoma, with parosteal and periosteal osteosarcomas being the most common. In contrast to the classical osteosarcoma, which arises within bone, parosteal and periosteal osteosarcomas arise in the surface of the bone.

Parosteal Osteosarcoma

Parosteal osteosarcoma is a distinct variant of osteosarcoma. Its prevalence is estimated to be 4%. It arises from the cortical bone and generally occurs in an older age group and has a better overall prognosis than osteosarcoma. As in osteosarcoma, the distal femur is the most common location; characteristically, the tumor attached to its posterior aspect. The proximal humerus and the proximal tibia are the next most frequent sites. Parosteal osteosarcomas usually present as a mass, occasionally associated with pain. The natural history is slow growth and late metastasis. The long-term survival rate is 75% to 85%. The tumor arises from the cortical surface and presents as a protuberant multinodular mass. The surface of the lesion may be covered in part by a cartilaginous cap resembling an osteochondroma; other areas may infiltrate into the adjacent soft tissues. The tumor usually encircles, partially or completely, the shaft of the underlying bone. In contrast to osteochondromas, the medullary canal of the bone is not contiguous with that of the neoplasm. Radiologically, parosteal osteosarcoma presents as a large, dense, tabulated mass that is broadly attached to the underlying bone without

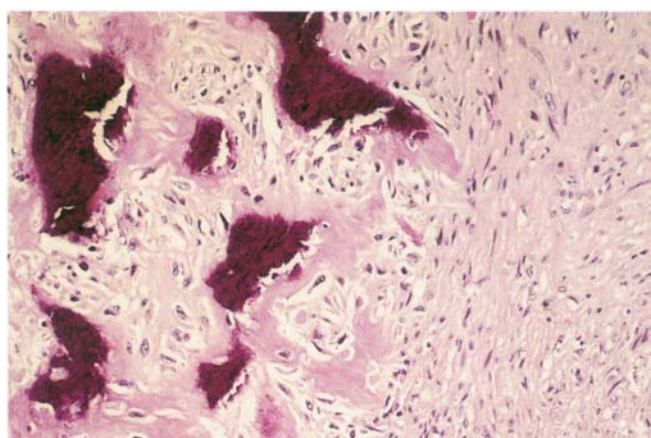


Figure 1.35 Classical high-grade osteosarcoma reveals a population of pleomorphic spindle cells intimately associated with a mesh of immature lacy osteoid. Occasionally the amount of osteoid can be minimal, or it may be a predominant element forming wide intersecting trabeculae lined by the malignant osteoblasts. Giant cells can also be present.

involvement of the medullary canal (Figure 1.36). If present long enough, the tumor may encircle the entire bone. The periphery of the lesion is typically less mature than the base. Despite careful evaluation, intramedullary extension is difficult to determine from the plain radiographs. It is more accurately detected with CT scan or MRI (Figure 1.37).

Diagnosis of parosteal osteosarcoma, more than that of other bone tumors, must be based on the clinical, radiological, and pathological findings. Most parosteal osteosarcomas are low-grade; they do not require neoadjuvant and adjuvant chemotherapy, and are best treated with wide excision. This tumor is commonly mistaken by inexperienced clinicians and pathologists as osteochondroma, myositis ossificans, or conventional osteosarcoma. In the classical low-grade lesion, irregularly formed osteoid trabeculae, usually of woven bone, are surrounded by a spindle-cell stroma containing widely spaced, bland-appearing fibroblastic spindle cells (Figure 1.38). With the higher grades the

likelihood of intramedullary involvement may be increased.

Periosteal Osteosarcoma

Periosteal osteosarcoma is a rare cortical variant of osteosarcoma that arises superficially on the cortex, most often on the tibial shaft. It projects into the adjacent soft tissues as a well-circumscribed tabulated mass. Radiologically, it is a small, radiolucent lesion with some evidence of bone spiculation. The cortex is characteristically intact with scooped-out appearance and a Codman's triangle (Figure 1.39). On section, the tumor reveals a dominant chondroid consistency. The histologic features are essentially those of intermediate-grade chondroblastic osteosarcoma. The cartilaginous lobules may contain markedly atypical chondrocytes. At the periphery of the lobule is situated a cellular spindle-cell component wherein a fine intercellular

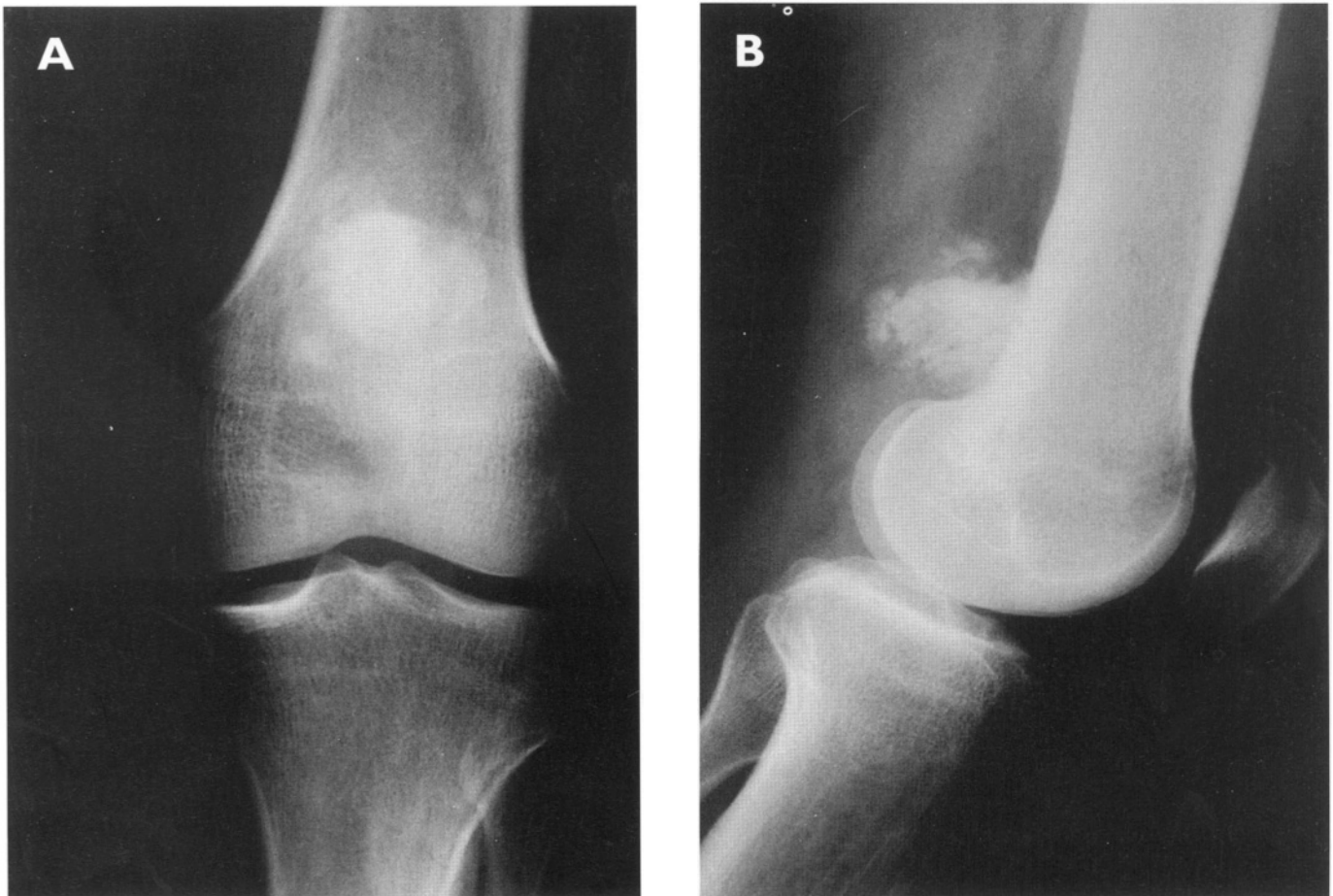


Figure 1.36 Parosteal osteosarcoma. Plain radiographs of the distal femur, (A) anteroposterior and (B) lateral views, show a dense, irregular, sclerotic lesion, attached to the posterior femoral cortex. The posterior aspect of the distal femur is a classical location for parosteal osteosarcomas and that diagnosis should be considered for any sclerotic lesion in that location.

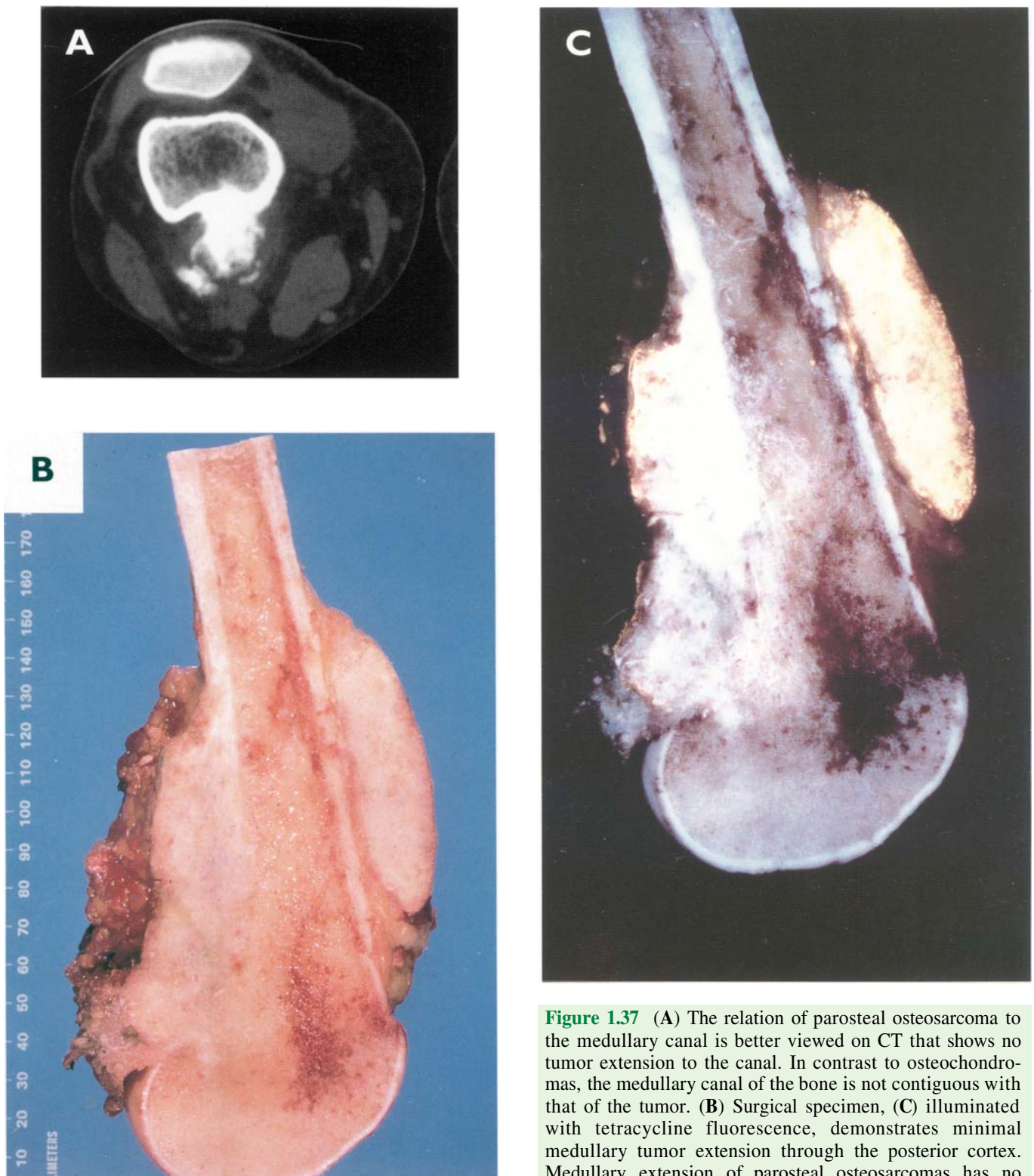


Figure 1.37 (A) The relation of parosteal osteosarcoma to the medullary canal is better viewed on CT that shows no tumor extension to the canal. In contrast to osteochondromas, the medullary canal of the bone is not contiguous with that of the tumor. (B) Surgical specimen, (C) illuminated with tetracycline fluorescence, demonstrates minimal medullary tumor extension through the posterior cortex. Medullary extension of parosteal osteosarcomas has no impact on survival; however, the extent of surgical resection must be changed to achieve wide margins.

osteoid matrix is produced. Areas of malignant osteoid and chondroid can be seen to infiltrate into the cortical bone at the base of the neoplasm.

Small-cell Osteosarcoma

In small-cell osteosarcoma the neoplastic cells are round rather than spindle-shaped. The tumor consists of nests and sheets of small round cells separated by fibrous septae, a pattern reminiscent of Ewing's sarcoma. Occasionally, transition to spindle cells is noted. The cells have well-defined borders and a distinct rim of cytoplasm. The round nuclei disclose a delicate chromatin pattern. The presence of a characteristic lace-like osteoid matrix, often surrounding individual or small nests of cells, confirms the diagnosis (Figure 1.40). The recommendations for treatment vary. Radiation and chemotherapy are used at some institutions while others choose primary surgical ablation with neoadjuvant and/or adjuvant chemotherapy. Too few cases have been reported to make definitive recommendations.

Chondrosarcoma

Chondrosarcoma is the second most common primary bone sarcoma. It is a heterogeneous group of tumors whose basic neoplastic tissue is cartilaginous and shows no evidence of primary osteoid formation. It is subdivided in a variety of ways, including by histological grade and by whether it is primary or secondary or peripheral or central. The single most

useful classification, both in terms of planning the surgical procedure and determining the prognosis, is histological grade. There are a few distinct, relatively rare, histological variants of chondrosarcoma. These include clear-cell, mesenchymal, and dedifferentiated chondrosarcoma.

Primary chondrosarcomas are not associated with a pre-existing lesion. Secondary chondrosarcomas are associated with a pre-existing chondroid lesion such as enchondroma, osteochondroma, chondroblastoma,

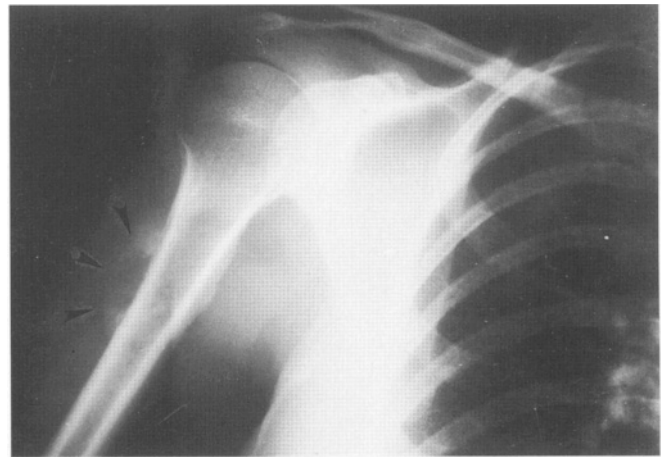


Figure 1.39 Periosteal osteosarcoma of the proximal humerus. Plain radiograph shows a typical "scooped-out" appearance of a cortical lesion (arrows). The center of the lesion has a lytic appearance because of its chondroblastic features. (Cancer: Principles & Practice of Oncology, 6th Edition, 2001; 39.2: 1891–1935)

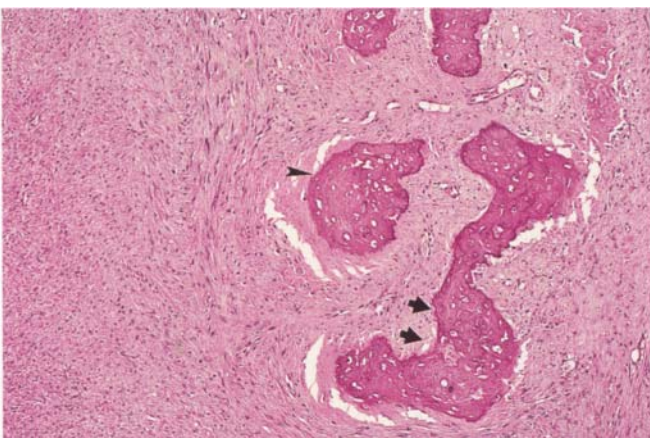


Figure 1.38 Parosteal osteosarcoma belongs to a group of bone surface sarcomas. It is usually a low-grade neoplasm. There are parallel or intersecting osseous trabeculae (arrows) that may be either lamellar or woven-bone-type matrix. The intervening fibrocollagenous tissue is composed of bland, widely spaced fibroblastic cells.

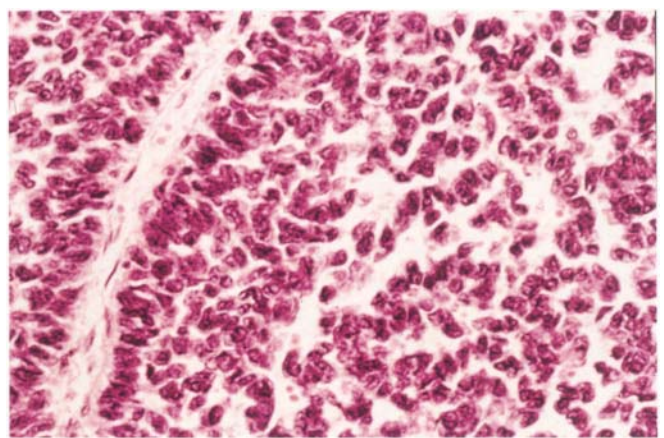


Figure 1.40 A rare variant of high-grade osteosarcoma is the so-called small-cell type. It is composed of small round blue cells, often with only sparse osteoid matrix to reveal the true diagnosis. Consequently extensive tumor sampling is necessary to differentiate it from Ewing's sarcoma, rhabdomyosarcoma, and lymphoma.

chondromyxofibroma, periosteal chondroma, and synovial chondromatosis (Figures 1.41, 1.42). Central chondrosarcomas arise from within the medullary canal, and peripheral chondrosarcomas arise from the surface of the bone. Primary chondrosarcomas are virtually always central; secondary chondrosarcomas can be central or peripheral. The treatment and prognosis of primary and central secondary chondrosarcomas are identical, and that distinction is made only to clarify the underlying pathogenesis.

The majority of the "conventional" chondrosarcomas occur between the ages of 40 and 60. The most common sites are the pelvis, femur, and shoulder girdle. Pelvic chondrosarcomas are often large and present with referred pain to the lower back, sciatic pain, urinary symptoms from pressure on the bladder neck, unilateral swelling of the lower extremity due to iliac vein obstruction, or a painless pelvic mass. Central chondrosarcomas usually present with pain. Correlation of the clinical, radiographic, and histological data is essential for accurate diagnosis and evaluation of the aggressiveness and metastatic potential of a cartilage tumor. In general, proximal or axial location, skeletal maturity, and pain point toward malignancy. Radiologically, central chondrosarcoma presents as a well-defined lytic lesion with a narrow zone of transition and surrounding sclerosis with faint calcification or with no sclerotic rim at all (Figure 1.43). Endosteal scalloping is the key sign of malignancy (Figure 1.44).

Central chondrosarcoma is an expansive lesion that commonly causes cortical destruction and subsequent extension to the soft tissues. Typically, the tumor

consists of fused, variably sized nodules that, on cut section, are composed of white-gray hyaline tissue, areas of calcification and even ossification. There may be focal myxoid areas (Figure 1.45).

The histological spectrum and the ease of diagnosis vary tremendously. High-grade tumors can be easily identified; in contrast, it may be exceedingly difficult to distinguish low-grade tumors from other benign cartilage tumors. When this diagnostic dilemma arises, correlation of the histological features with both the

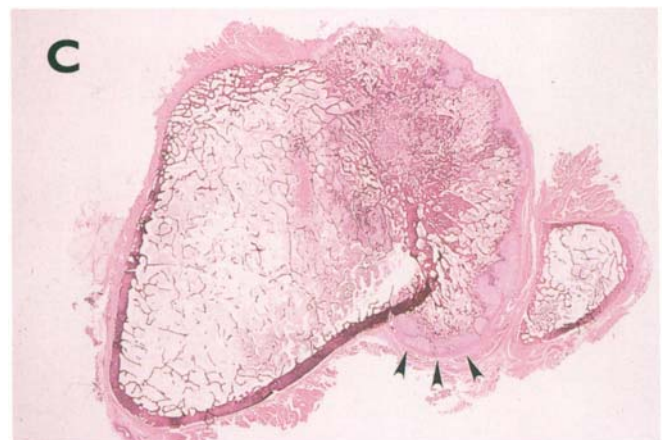
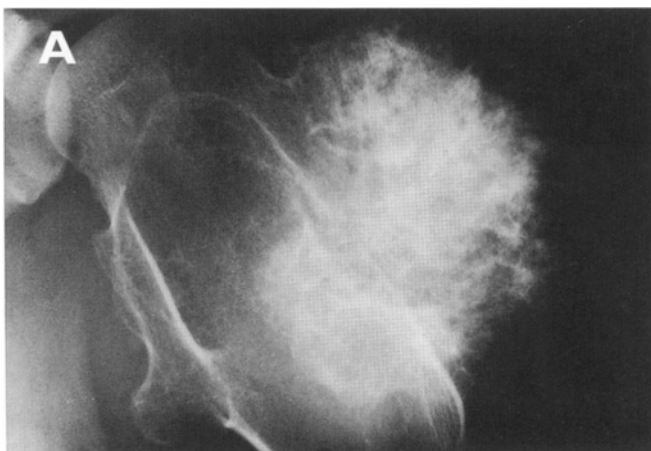


Figure 1.41 Secondary, low-grade chondrosarcomas, arising from osteochondromas of the (A) proximal humerus, (B) proximal femur, and (C) proximal tibia (arrows point to the region of the cartilage cap that has undergone malignant transformation).

clinical setting and the radiographic changes becomes extremely important. Chondrosarcomas are histologically graded as I (low), II (intermediate), or III (high); the majority are grade I or II. Grade I tumors are characterized by a slightly increased number of chondrocytes, set in lobular chondroid matrix. The cells contain hyperchromatic nuclei, occasionally binucleate forms that show minimal variation in size (Figure 1.46). Areas of markedly increased cellularity with more prominent pleomorphism and significant nuclear atypia define a grade II tumor. Myxoid matrix changes are indicative of a grade II tumor, or even higher. Grade III chondrosarcoma, which accounts for approximately 10% of all chondrosarcomas, discloses greater cellularity, often with spindle-cell areas, and prominent mitotic activity. Areas of myxoid changes are common, and the malignant chondrocytes may contain large, bizarre nuclei (Figure 1.47). Calcification and enchondral ossification can be observed in tumors of all grades; however, the presence of unequivocal malignant osteoid production, even in the face of chondrosarcomatous areas, dictates that the tumor be classified as osteosarcoma.

Resection is the treatment of choice for all chondrosarcomas. Low-grade chondrosarcomas or enchondrosarcomas may be treated by intralesional resection. Curettage, burr drilling, and, in most cases, the use of adjuvant liquid nitrogen should be considered. Intermediate- and high-grade chondrosarcomas, on the other hand, are treated surgically by wide resection. The use of neoadjuvant and adjuvant chemotherapy for chondrosarcomas is controversial. Low- and intermediate-grade chondrosarcomas

respond poorly to chemotherapy. Although there are few data on the efficacy of chemotherapy in the treatment of high-grade chondrosarcomas, it should be considered in any young patient with a high-grade tumor. Radiation is recommended when anything other than wide excision is performed for a chondrosarcoma of any grade.

Ewing's Sarcoma

Ewing's sarcoma is a distinct round-cell sarcoma that occurs predominantly in the long bones of skeletally immature patients. The tumor is composed of undifferentiated, round, mesenchymal cells that are rich in glycogen and typically manifest a unique reciprocal chromosomal translocation, $t(11;22)(q24;q12)$ that results in a chimeric protein, EWS/FLI-1. This translocation occurs in approximately 90% of these tumors. Very few other human tumors exhibit such consistent karyotypic alterations, which might play a significant role in their pathogenesis.

Ewing's sarcoma is the third most common primary bone sarcoma. It has a significant predilection for the White population; it is rare to diagnose Ewing's sarcoma in a Black patient. The peak incidence is the second decade of life. In very young patients, and in patients over the age of 30, a diagnosis of Ewing's sarcoma should be questioned, because it occurs so rarely in these age groups. Common differential diagnoses include metastatic neuroblastoma and acute leukemia (in the young age group) and small-cell carcinoma and large-cell lymphoma (in patients older than 30). With the advent of molecular probes and

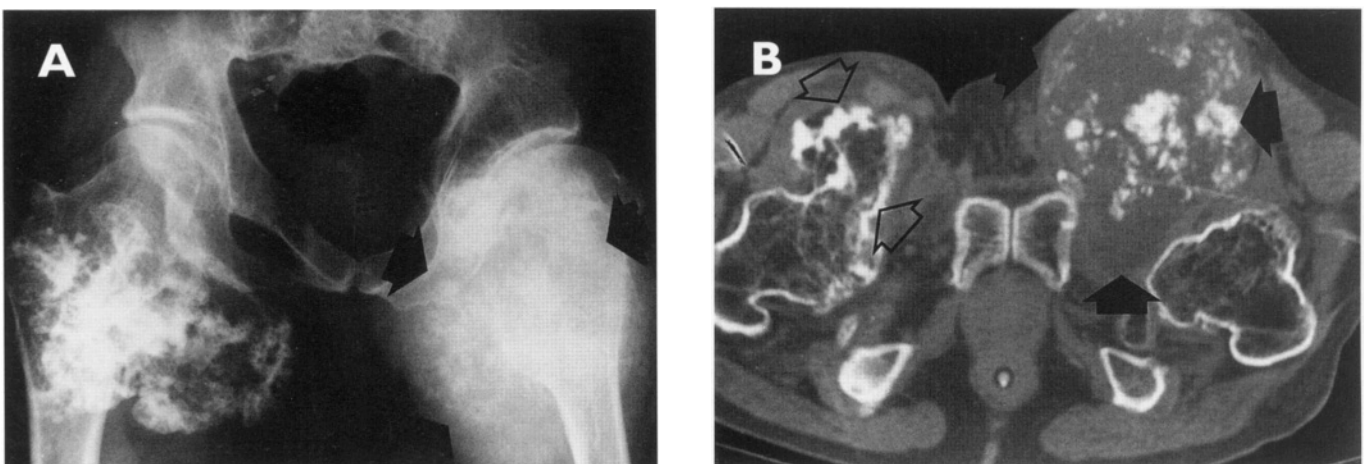


Figure 1.42 Secondary chondrosarcoma arising from the left proximal femur in a patient with multiple hereditary exostosis. (A) Plain radiograph shows a large, benign-appearing osteochondroma arising from the right proximal femur and a large, poorly demarcated cartilage tumor, arising from the left (solid arrows). (B) CT shows a marked difference between the two lesions. The destructive neoplastic tissue (solid arrows) has completely replaced the osteochondroma on the left, and it is almost fungating through the skin. The patient underwent modified hemipelvectomy and remains disease-free after more than 10 years of follow-up. (Cancer: Principles & Practice of Oncology, 6th Edition, 2001; 39.2: 1891–1935)

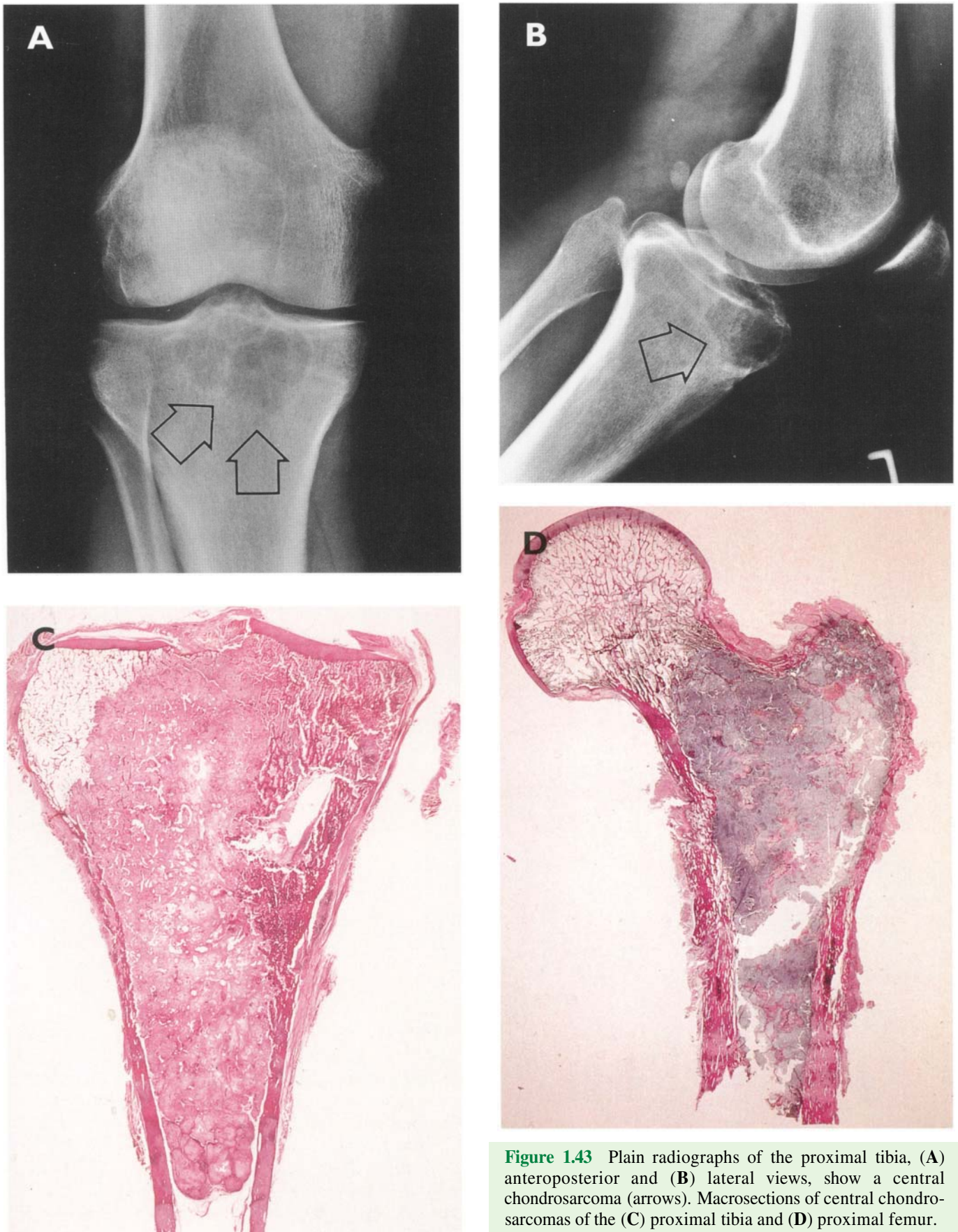


Figure 1.43 Plain radiographs of the proximal tibia, (A) anteroposterior and (B) lateral views, show a central chondrosarcoma (arrows). Macrosections of central chondrosarcomas of the (C) proximal tibia and (D) proximal femur.

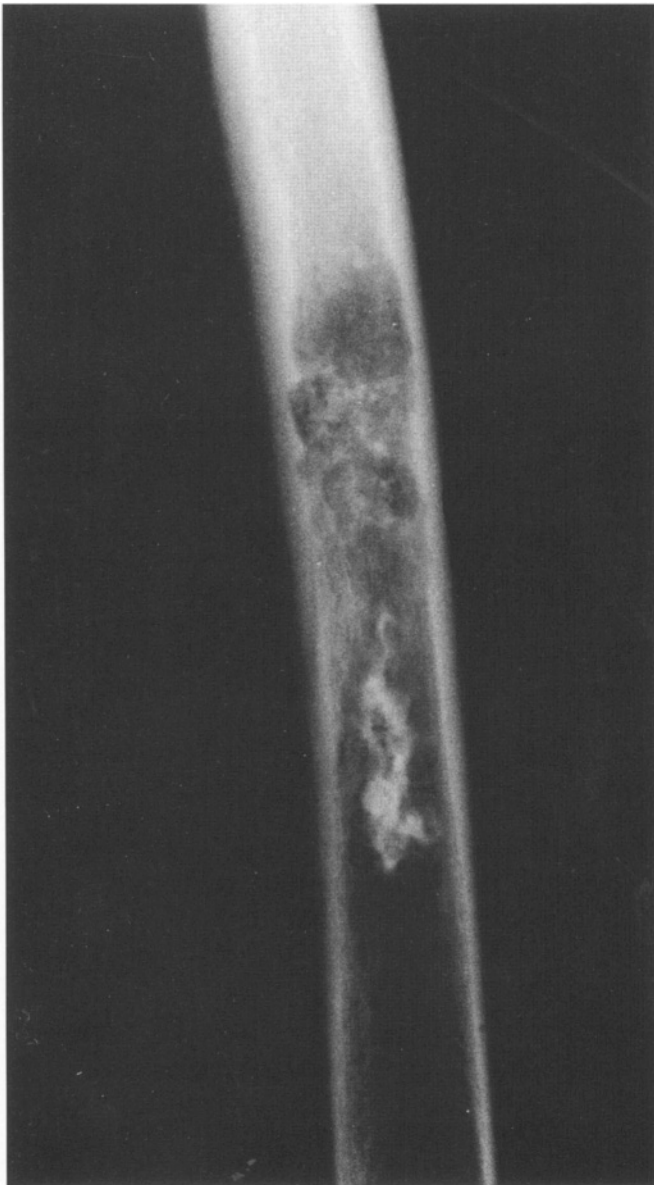


Figure 1.44 Plain radiograph of the femoral shaft, showing a central chondrosarcoma, presenting as a well-defined lytic lesion with a sharp transition zone, calcifications, and endosteal scalloping.

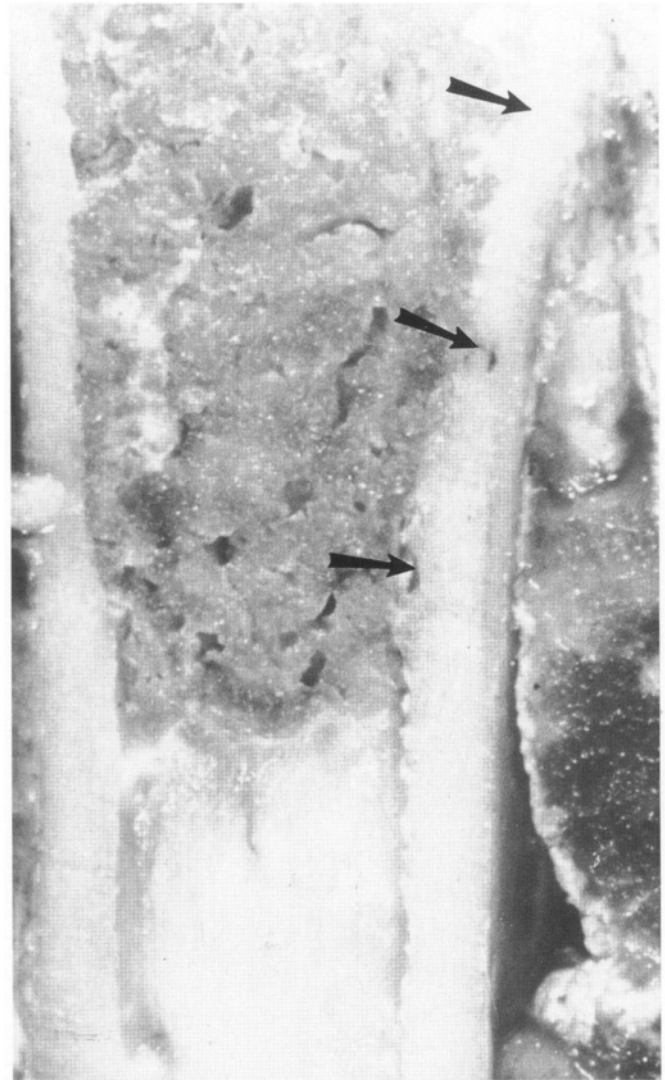


Figure 1.45 Cross-section of an intramedullary chondrosarcoma discloses its lobular architecture and translucent, hyaline-like matrix. Note the characteristic endosteal erosions (arrows).

immunohistochemical stains, differentiation among these tumors has become simpler.

Radiologically, Ewing's sarcoma presents as an ill-defined, permeative or focally moth-eaten, destructive intramedullary lesion that affects the diaphysis. Ewing's sarcomas are frequently lytic or have a mixed pattern; however, in approximately 15% of the cases a sclerotic appearance is dominant. Ewing's sarcomas are associated with a diffuse, irregular, and wavy periosteal reaction consisting of multiple parallel layers. That

reaction has been named "onion-skin appearance". The large majority of these tumors break through the cortex and have an extensive soft-tissue component (Figure 1.48). Histologically, the small round cells grow in solid, densely packed sheets and nests that fill the intertrabecular spaces. They have round, centrally located nuclei with indistinct cytoplasmic features. The nuclear chromatin is granular, and there are usually one to three clearly identifiable small- to intermediate-sized nucleoli (Figure 1.49). Often a biphasic pattern is simulated by the presence of "light" and "dark" cells (i.e., cells with an open chromatin structure and cells with dark condensed nuclei, respectively). The latter represent apoptotic tumor cells. The ratio between light

and dark cells varies from tumor to tumor and even in different areas of the same lesion.

Ewing's sarcoma is an extremely malignant tumor with high rates of metastatic disease and local recurrence following surgery alone. The 5-year survival rate has risen dramatically, from 5% to more than 60%, because of the use of multimodality treatment that includes chemotherapy, surgery, and radiation therapy in selected cases in which wide margins were not or could not be achieved at surgery. As with any high-grade primary bone sarcoma, the surgical aim is wide resection.

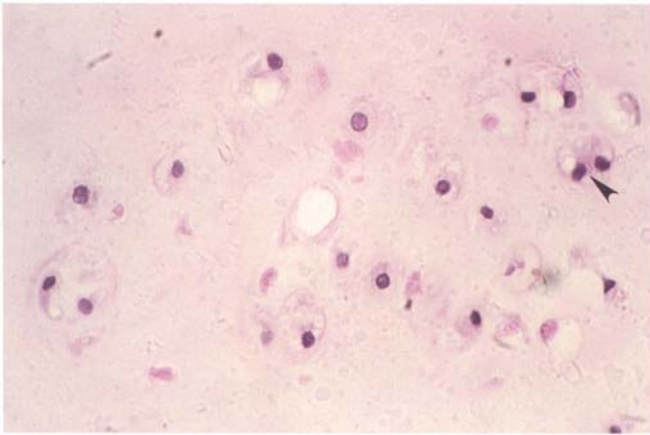


Figure 1.46 Low-grade chondrosarcoma maintains a lobular architecture. There is slightly increased cellularity, occasional binucleate cells (arrow) and nuclear atypia. These cells are typically found in lacunae. The tumor tends to permeate between the normal osseous trabeculae.

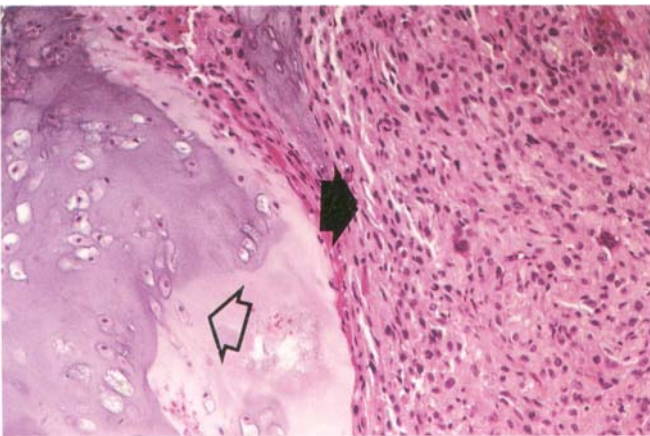


Figure 1.47 The juxtaposition of high-grade spindle sarcoma (solid arrow) with lobules of low-grade chondrosarcoma (open arrow) is the hallmark of dedifferentiated chondrosarcoma. The spindle-cell component usually reveals features of malignant fibrous histiocytoma, osteosarcoma, or it may be unclassifiable. This neoplasm pursues an aggressive clinical course with very low long-term survival.

Giant-cell Tumor of Bone

Giant-cell tumor (GCT) is a locally aggressive tumor with a low metastatic potential. It occurs slightly more often in females than in males. The primary areas of involvement are the femoral condyles, tibial plateau, proximal humerus, and distal radius. The tumor is thought to arise in the metaphyseal–epiphyseal junction. Large tumors may extend into the metaphysis and, more rarely, into the diaphysis. GCT occasionally occurs in the vertebrae and sacrum. The descriptor “benign” was first applied to GCT to differentiate it from other bony malignancies that required amputation. The quotation marks were gradually removed and GCT is now considered a benign aggressive lesion. This descriptor is misleading, because 3% of GCTs are primarily malignant or will undergo malignant transformation either after radiation therapy or after several local recurrences. GCT is, therefore, considered by the authors to be a low-grade primary bone sarcoma and is treated as such.

Radiologically, GCTs are eccentric lytic lesions without matrix formation. They have well-defined borders and a very sharp transition between the tumor and the host bone. Periosteal elevation is rare unless a pathological fracture is present (Figure 1.50). Expanded and thinned cortex and, occasionally, cortical breakthrough and soft-tissue extension are common (Figure 1.51). Histologically, two basic cell types comprise the typical GCT. The stroma consists of polygonal to somewhat spindle cells containing central round nuclei. Typical mitotic figures, sometimes numerous, are often noted. Scattered diffusely throughout the stroma are benign osteoclast-like giant cells (Figure 1.52). Small foci of osteoid matrix, produced by the stromal cells, can be observed. Chondroid matrix never occurs. Extensive hemorrhage, pathologic fracture, or previous surgery can alter significantly the usual histologic picture of GCT and make it resemble a primary bone sarcoma. These events must be recognized at the time of histologic interpretation in order to prevent diagnostic errors. Cystic areas with surrounding hemosiderin pigment and xanthoma cells correspond to the grossly observed cyst. A malignant GCT contains areas of unequivocal sarcomatous transformation, usually typical of fibrosarcoma or osteosarcoma. The sarcomatous component is devoid of ordinary GCT features; thus, it is only by the recognition of foci of residual GCT, or by the confirmation of pre-existing GCT, that an accurate diagnosis of malignant GCT can be established.

Treatment of GCT is surgical removal. During the past several decades, surgeons have used the following: (1) curettage; (2) curettage and cytotoxic agents such as phenol, zinc chloride, alcohol, H_2O_2 , or



Figure 1.48 (above and above right) (A) CT scan of a Ewing's sarcoma of the scapula demonstrating a large soft-tissue (extraosseous) component. Ewing's sarcomas often have a large soft-tissue component, especially when a flat bone is involved. (B) Gross photograph of a Ewing's sarcoma of the scapula following resection. Note the large soft-tissue extension both anteriorly and posteriorly to the glenoid.

carbolic acid; (3) curettage and a physical adjuvant (polymethylmethacrylate and cryosurgery); (4) primary resection; (5) radiation therapy; and (6) embolization, which is practiced in unresectable tumors. Simple curettage, with or without cytotoxic agents, has a significantly high rate of local recurrence of up to 57%. Treatment of GCT with curettage, burr drilling, and cryosurgery using application of liquid nitrogen to the tumor cavity has achieved a recurrence rate of less than 3% among patients who were primarily treated with that modality. This is among the lowest reported recurrence rate after any surgical intervention for GCT of bone. Cryosurgery is, therefore, recommended as a physical adjuvant to curettage in the treatment of GCTs of bone.

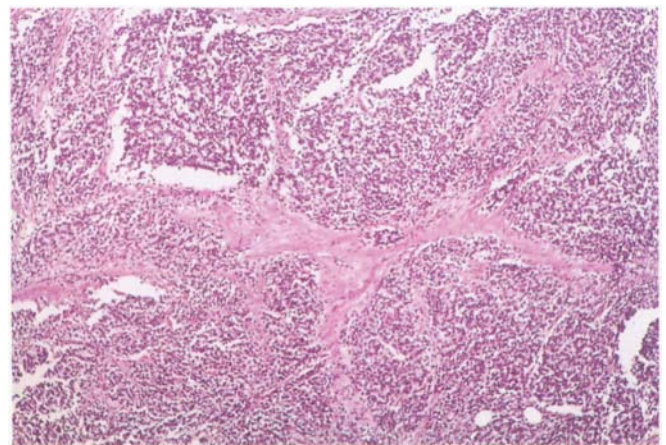


Figure 1.49 Ewing's sarcoma belongs to the ever-expanding category of small, round, blue-cell tumors. It is composed of round cells with scanty cytoplasm and round to oval nuclei. The nuclear chromatin tends to be fine homogeneous. Differentiation from the other members of the round-cell family may require the use of immunohistochemistry, electron microscopy, and cytogenetic and oncogene markers.

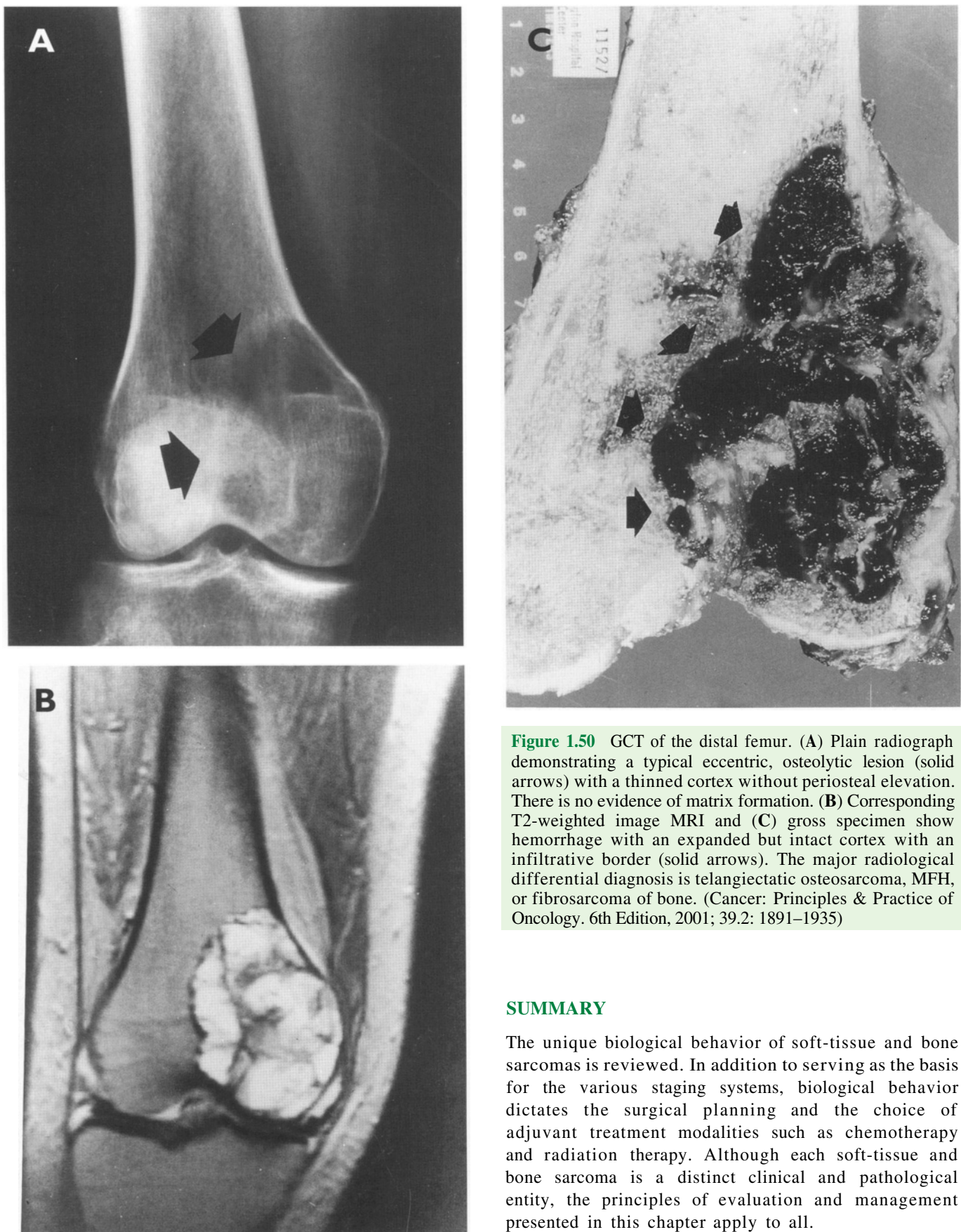


Figure 1.50 GCT of the distal femur. (A) Plain radiograph demonstrating a typical eccentric, osteolytic lesion (solid arrows) with a thinned cortex without periosteal elevation. There is no evidence of matrix formation. (B) Corresponding T2-weighted image MRI and (C) gross specimen show hemorrhage with an expanded but intact cortex with an infiltrative border (solid arrows). The major radiological differential diagnosis is telangiectatic osteosarcoma, MFH, or fibrosarcoma of bone. (Cancer: Principles & Practice of Oncology, 6th Edition, 2001; 39.2: 1891–1935)

SUMMARY

The unique biological behavior of soft-tissue and bone sarcomas is reviewed. In addition to serving as the basis for the various staging systems, biological behavior dictates the surgical planning and the choice of adjuvant treatment modalities such as chemotherapy and radiation therapy. Although each soft-tissue and bone sarcoma is a distinct clinical and pathological entity, the principles of evaluation and management presented in this chapter apply to all.



Figure 1.51 Macrosection of the proximal femur, showing giant-cell tumor of bone (solid arrows) with cortical breakthrough and extension to the surrounding soft tissues. A tract from a hip screw is seen extending from the femoral head to the lateral cortex. This patient was treated by resection and proximal femoral prosthesis.

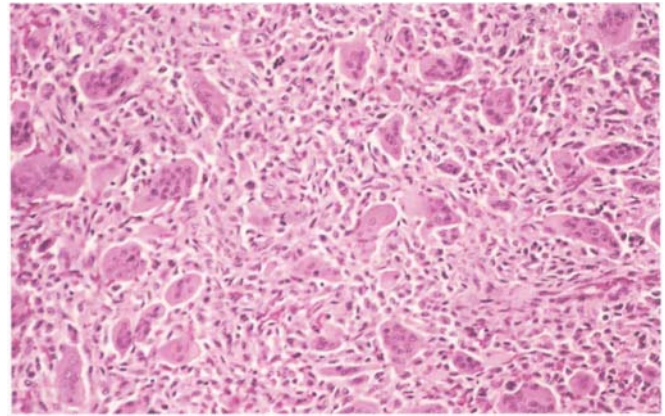


Figure 1.52 Giant-cell tumor of bone reveals a rather uniform distribution of osteoclastic giant cells. The background contains round to polygonal histiocytic cells. Normal mitotic figures can be seen. Hemorrhage with aneurysmal bone cyst changes is not unusual.

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2

Biopsy of Musculoskeletal Tumors

**Jacob Bickels, James Jelinek, Barry Shmookler and
Martin Malawer**

OVERVIEW

Biopsy is a key step in the diagnosis of bone and soft-tissue tumors. An inadequately performed biopsy may fail to allow proper diagnosis, have a negative impact on survival, and ultimately necessitate an amputation to accomplish adequate margins of resection. Poorly performed biopsy remains a common finding in patients with musculoskeletal tumors who are referred to orthopedic oncology centers. The principles by which an adequate and safe biopsy of musculoskeletal tumors should be planned and executed are reviewed and a surgical approach to different anatomic locations is emphasized.

INTRODUCTION

Biopsy is a key step in the diagnosis of a musculoskeletal tumor. In a book published in 1958, Jaffe stated that a biopsy should be regarded as the final diagnostic procedure, not as a mere short cut to diagnosis.¹ Biopsy must be preceded by careful clinical evaluation and analysis of the imaging studies. The diagnosis of a musculoskeletal lesion is based on these three parameters; all three have to fit and the diagnosis must be questioned when they do not match.¹ In the past, biopsies were performed routinely through a large incision with significant contamination of the surrounding soft tissues with tumor cells. The contamination, however, had minimal significance because most malignant tumors of the extremities and pelvis were treated with amputation. Today, limb-sparing procedures are performed in 90–95% of patients with musculoskeletal tumors of the extremities, and indications and surgical technique of musculoskeletal biopsy had to be changed to allow these procedures to be performed.^{2,3}

The presence of a bone or soft-tissue lesion does not necessarily merit a biopsy. The combination of medical history, thorough physical examination, laboratory data when indicated, and appropriate imaging studies allows accurate diagnosis of most musculoskeletal lesions. Clinically and radiologically benign-appearing lesions do not have to have a biopsy. In contrast, biopsy is indicated in benign aggressive, malignant, and questionable lesions to confirm the clinical diagnosis and accurately classify the lesion before initiation of definitive treatment.

Technically, most biopsies are simple. Decisions regarding the indication for biopsy, the specific region of the lesion that has to have a biopsy, and the anatomic approach and biopsy technique can make the difference between a successful biopsy and a catastrophe. A poorly performed biopsy could become an obstacle to proper diagnosis and may have a negative impact on survival. Furthermore, patients who have undergone poorly performed biopsies subsequently may require an amputation to achieve an adequate surgical resection.

In 1982, Mankin *et al.*⁴ evaluated 329 patients who underwent biopsy for bone or soft-tissue sarcomas. The rate of major errors in diagnosis was 18.2%, and the rate of complications was 17.3%. Unnecessary amputations were performed in 4.5% of these patients.⁴ These events were found to occur with far greater frequency when the biopsy was performed in a referring institution rather than in a specialized oncology center. In addition to technical recommendations (most of which will be discussed in this chapter), it was

recommended that if a surgeon or an institution is not equipped to perform accurate diagnostic studies or definitive surgery and adjunctive treatment of musculoskeletal tumors, the patient should be referred to a specialized treating center before the biopsy is performed.⁴ In 1996, Mankin *et al.*⁵ performed a second study on 597 patients. They documented major errors in diagnosis in 13.5% of the patients, a complication rate of 15.9%, and unnecessary amputations in 3%. The differences in outcome between referring and oncology centers were unchanged and their recommendation was identical.⁵

The current chapter reviews the principles according to which a safe and adequate biopsy of bone and soft-tissue tumors should be planned and performed.

BIOLOGY OF MUSCULOSKELETAL TUMORS

Because of the common origin from the mesenchymal elements of the musculoskeletal system, bone and soft-tissue sarcomas share certain unique biologic characteristics. Sarcomas grow in a centripetal fashion with the most immature part of the lesion at the growing edge. A reactive zone is formed between the tumor and the compressed surrounding normal tissues. The reactive zone is composed of induced proliferation of mesenchymal cells, neovasculation, and inflammatory process.⁶ The type of mesenchymal proliferation is determined by the anatomic location of the tumor: soft-tissue tumors stimulate a fibrous reaction, and intraosseous lesions stimulate a bone-forming reaction. Furthermore, the same lesion in different areas will stimulate different mesenchymal responses. The reactive region around an intraosseous lesion matures into reactive bone, whereas if the lesion penetrates the soft tissues, the mesenchymal response is fibrous.^{6,7} Unlike sarcomas, carcinomas usually infiltrate, rather than push, the surrounding tissues and usually do not induce the formation of a reactive zone.⁸

The reactive zone may be invaded by tumor nodules that represent microextensions of tumor. These nodules are termed satellites and are not a metastatic phenomenon. High-grade sarcomas may present with tumor nodules that grow outside the reactive rim but within the same anatomic compartment in which the lesion is located. These nodules are termed skip lesions (Figures 2.1, 2.2).^{2,7} Low-grade sarcomas rarely manifest with skip lesions.⁶ Metastatic disease from bone and soft-tissue sarcomas is site-specific; it is manifested by lung involvement in its early stage and secondarily by bone involvement.^{2,9}

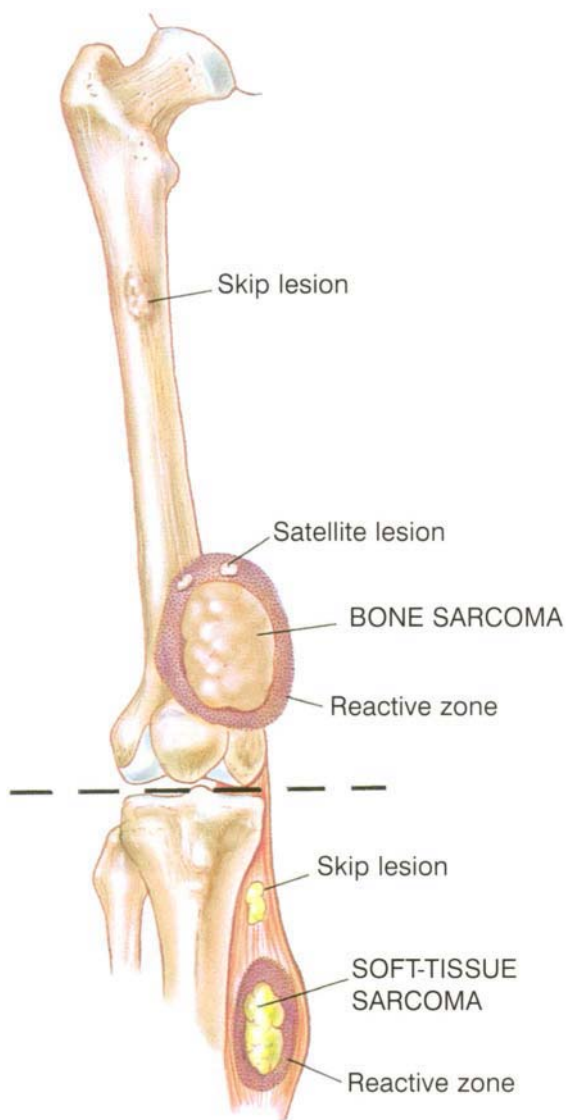


Figure 2.1 Growth pattern of bone and soft-tissue sarcomas. Sarcomas grow in a centripetal fashion, with the most immature part of the lesion at the growing edge. A reactive zone is formed between the tumor and the compressed surrounding normal tissues and may be invaded by tumor nodules that represent microextensions of tumor (satellites) and are not a metastatic phenomenon. High-grade sarcomas may present with tumor nodules that grow outside the reactive zone (skip lesions) but within the same anatomic compartment in which the lesion is located. (Clin Orthop 1999 Nov; (368): 212–219)

DIAGNOSTIC STUDIES AND BIOPSY CONSIDERATIONS

Biopsy of a musculoskeletal lesion should be performed only at the conclusion of staging, which is the process that entails performing the imaging studies required to determine the characteristics and local extent of the tumor and the presence of metastatic disease. Staging

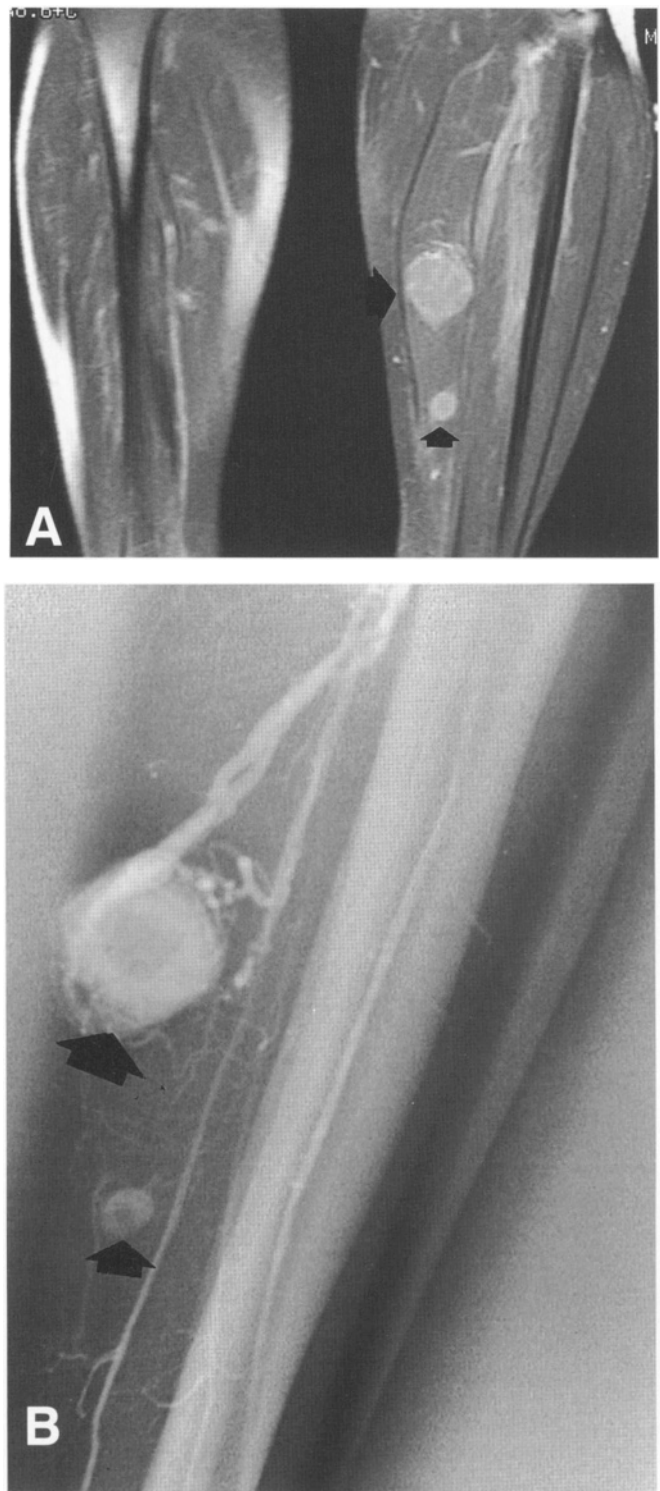


Figure 2.2 A 40-year-old woman presented with a rapidly enlarging mass that had developed in her calf. Physical examination revealed a deep-seated, firm mass, 10 cm in diameter, located at the proximal aspect of the calf. (A) Magnetic resonance imaging revealed the primary lesion and additional skip metastasis (small arrow) in the substance of the soleus muscle. Core needle biopsy of the primary lesion established the diagnosis of a high-grade leiomyosarcoma. (B) The skip metastasis (small arrow) is shown clearly in an angiogram performed before radical excision of the tumors. The large arrow represents the primary tumor

helps determine the exact anatomic approach to the tumor and specifies the region of the tumor that represents the underlying disease. A final reason for deferring biopsy until staging is complete is that biopsy superimposes real and artificial radiologic changes at the biopsy site, and therefore can alter the interpretation of the imaging studies.

Anatomic Location of the Biopsy Tract

The position of the biopsy site within the lesion has a major significance because bone and soft-tissue tumors may have regional morphologic variations.^{2,6,7} As a result of that heterogeneity, multiple samples are required to establish a diagnosis. Carcinomas, by contrast, are commonly homogeneous and a single tissue core or aspirate is sufficient for diagnosis. The term "sampling error" refers to an incorrect or inconclusive diagnosis that occurs because the biopsy specimen was taken from a region that does not represent the underlying primary disease. The clinical findings and imaging studies must be evaluated before biopsy by the surgeon and the radiologist, who must be familiar with the biologic and radiologic findings of musculoskeletal tumors. The questions that must be answered before biopsy are: (1) What part of the lesion has to have a biopsy? and (2) What is the safest anatomic route to that location?

Despite serious concerns regarding the potential of accelerated growth or metastatic dissemination of a malignant tumor after biopsy, there is no well-founded, objective evidence that biopsy promotes either adverse event. The real risk of open and needle biopsies is that they may spread tumor cells locally and facilitate local tumor recurrence (Figure 2.3).^{10–13} The actual risk of local recurrence after biopsy is not well documented, but it is reasonable to assume that it is higher in open biopsy than in needle biopsy, and that it is related to the width of the biopsy tract and adequacy of homeostasis. In planning the definitive surgery it must be assumed that the biopsy tract is contaminated with tumor cells and, therefore, it should be resected with the same safety margins as the primary tumor (i.e., wide margins – Figure 2.4).

For these reasons the surgeon performing the biopsy must be familiar with the technique of the potential definitive procedure, whether it is limb-sparing surgery or amputation. The biopsy incision or the needle puncture hole, and the tract to the tumor, must be made with the planned surgical incision site so that they will be included within the surgical specimen. Preferably, the surgeon performing the biopsy will be the same person who will perform the definitive procedure.

General guidelines regarding positioning of the biopsy tract are applicable to biopsies of bone and soft-

tissue lesions and are independent of the technique (open versus needle biopsy) and anatomic location. These guidelines can be summarized as follows: (1) Decide, before biopsy, what part of the lesion is most representative of the underlying disease and will need to have a biopsy. As a rule, the extraosseous component of a malignant bone tumor is as representative of the tumor as is the bony component, and should have biopsy, if present. Violating the cortex of a bone that harbors a malignant tumor, predisposes the patient to a pathologic fracture, and is recommended only if there is no extraosseous extension of the tumor. (2) Position the point of entry along the planned incision of the definitive surgery. (3) The biopsy tract must be the shortest way to the lesion; however, it must not violate more than one compartment and must be as remote as possible from the main neurovascular bundle of the extremity. Figures 2.5–2.7 show the recommended surgical approach to the four most common locations of primary bone sarcomas (proximal femur, distal femur, proximal tibia, and proximal humerus).

Biopsy Technique

A closed biopsy does not involve an incision. The specimen is obtained after skin puncture by a needle or trephine. An open biopsy, in contrast, requires an incision. It can either be incisional, in which case only a representative specimen is removed from the lesion, or excisional, in which the lesion is excised en-bloc. Any surgical procedure, even the most minor, is accompanied by a risk of complications that may include iatrogenic injury to blood vessels or nerves, complicated wound healing, wound infection, and tumor cell contamination along the biopsy tract and subsequent local recurrence.

Open incisional biopsy is a reliable diagnostic method because it allows the pathologist to evaluate cellular morphologic features and tissue architecture from different sites of the lesion. Furthermore, it provides material for performing ancillary studies such as immunohistochemistry, cytogenetics, molecular genetics, flow cytometry, and electron microscopy. These studies may help in the diagnosis and subclassification of bone and soft-tissue tumors, and therefore guide the definitive treatment.

Needle biopsy of mesenchymal tumors initially was criticized because the quantity of biopsy material was often insufficient for routine histopathologic evaluation and ancillary studies that require tissue. Fine-needle aspiration (FNA) using a 22-gauge needle, has been shown to be a reliable technique for the diagnosis of soft-tissue tumors that also provides sufficient material for additional studies.^{14–20} Diagnostic accuracy of FNA is highest when the cell type of the tumor is homogeneous,

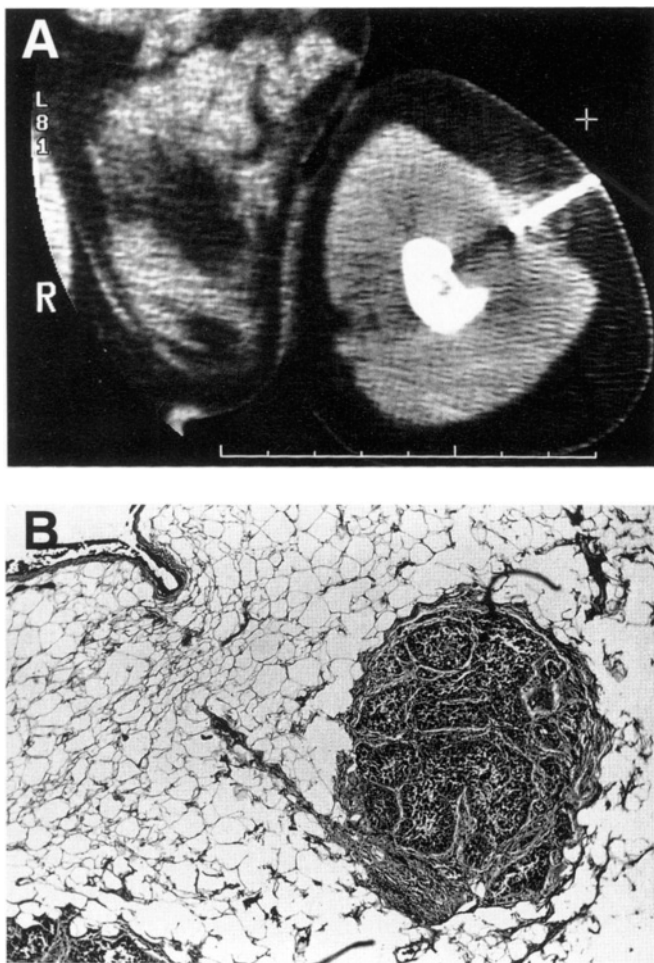


Figure 2.3 (A) Computed tomography guided core needle biopsy of a lytic lesion of the distal humerus, suspected of being a metastatic malignant melanoma. (B) That patient underwent resection–curettage and cryosurgery, followed by radiation therapy. The biopsy tract was resected en-bloc and its pathological evaluation revealed a tumor deposit.

as in the case of multiple myeloma or metastatic carcinomas. Tissue architecture and matrix formation have a major significance in the histologic evaluation and diagnosis of bone tumors. An important limitation of FNA stems from its inability to sample tissue matrix adequately and to show tumor structure.¹⁶ Because of these considerations, with the exception of few specialized centers,^{14,21,22} FNA is not commonly used to diagnose primary bone tumors.²³

Core needle biopsy (CNB), using a 14-gauge needle that provides a core of tissue with a maximum length of 20 mm, was shown to be more than 90% accurate in differentiating malignant from benign lesions.²⁴ In most patients with suspected bone or soft-tissue sarcomas it is the biopsy performed before initiation of treatment. Core needle biopsy is commonly practiced as the first

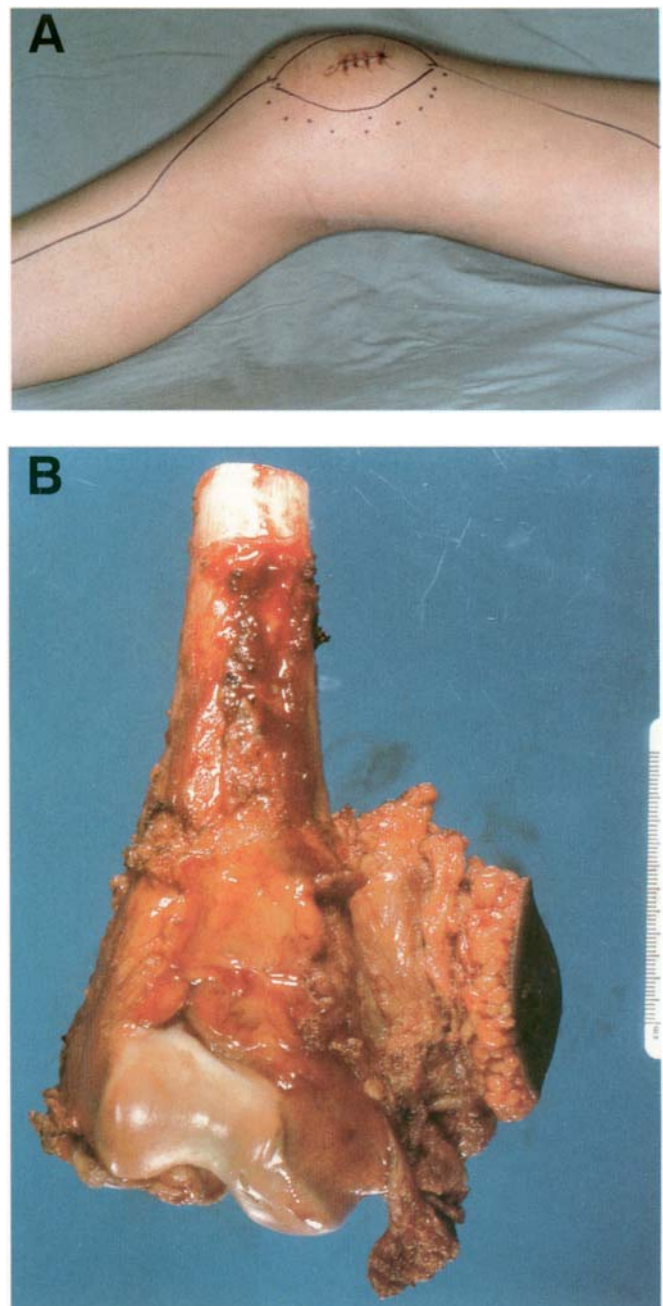


Figure 2.4 (A) Biopsy site over an osteosarcoma of the distal femur. The definitive surgical incision is planned to include the biopsy skin incision and the biopsy tract. (B) The tumor is resected en-bloc with the biopsy tract and the biopsy skin incision.

biopsy modality.²⁴ Open biopsy is performed when the pathologic diagnosis either is inconclusive or does not correlate with the clinical presentation and radiologic findings. Bone biopsies, using a CNB, should be performed under CT or fluoroscopy guidance, and multiple cores should be obtained. Biopsy of a deep-

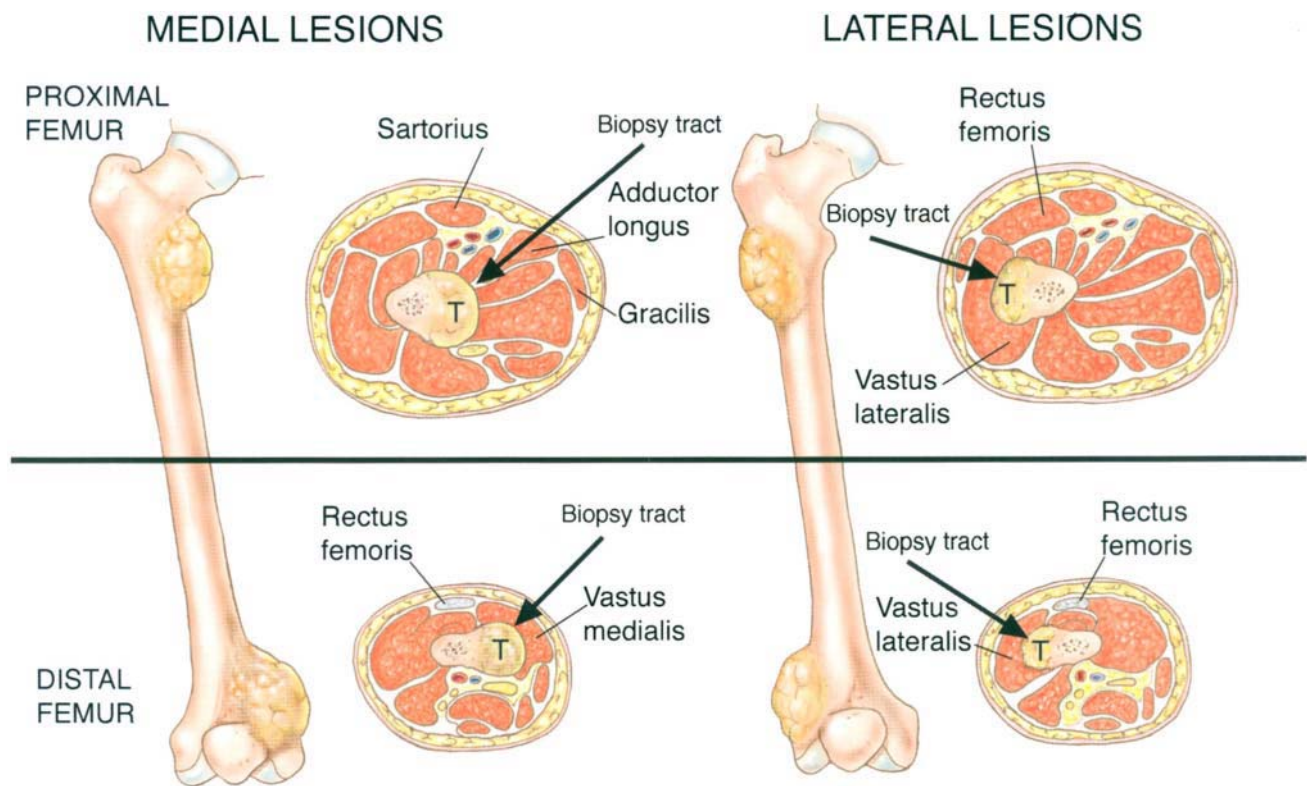


Figure 2.5 Biopsy tract, proximal and distal femur. A distinction is made between lateral and medial lesions. Because the majority of primary bone sarcomas have an extraosseous extension, the muscle underlying the tumor has to be resected with the specimen. This principle applies to all anatomic locations. (Clin Orthop 1999 Nov; (368): 212–219)

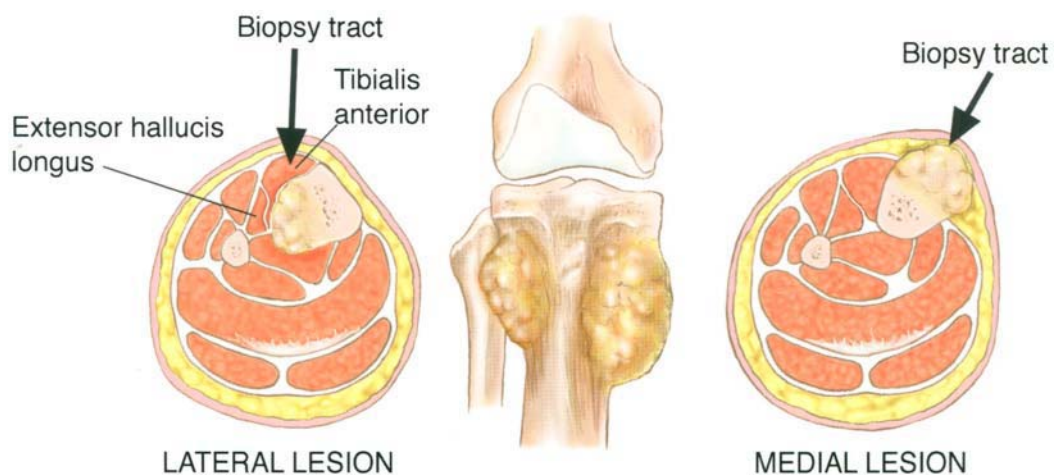


Figure 2.6 Biopsy tract, proximal tibia. (Clin Orthop 1999 Nov; (368): 212–219)

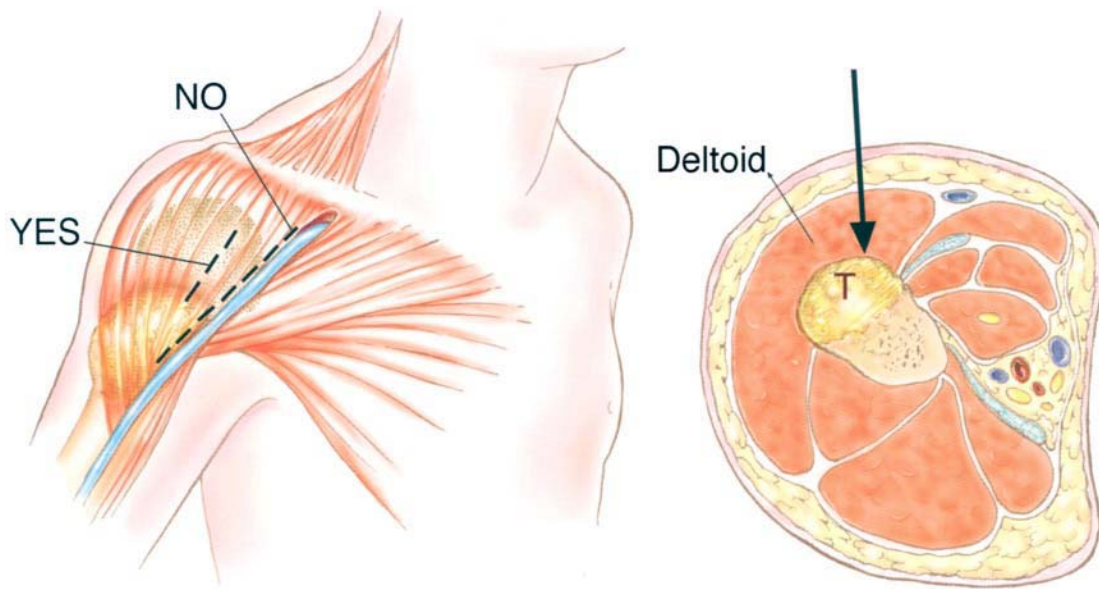


Figure 2.7 Biopsy tract, proximal humerus. The deltoid muscle has to be resected with most primary bone sarcomas of the proximal humerus. A transdeltoid approach through the anterior third of the muscle is used. The traditional deltopectoral approach will necessitate wider resection of the pectoralis major muscle, compromise its use for soft-tissue reconstruction, and may contaminate the main neurovascular bundle of the upper extremity. (Clin Orthop 1999 Nov; (368): 212–219)

seated or pelvic soft-tissue tumors is performed under CT guidance. If a soft-tissue tumor is palpable and is remote from the neurovascular bundle, a biopsy can be performed in a clinic setting.

After adequate planning of the biopsy tract, biopsy should be executed according to the following guidelines: (1) Use the smallest longitudinal incision that is compatible with obtaining an adequate specimen. Transverse incisions are contraindicated because they require a wider soft-tissue resection at the time of definitive surgery (Figure 2.8). (2) Use a knife or curette to avoid crushing or distorting the specimen's texture. When a purely intraosseous bone lesion is having biopsy, make a cortical window and pay attention to its shape. Clark *et al.*²⁵ evaluated the impact of three types of hole shape (rectangular hole with square corners, rectangular hole with rounded corners, and oblong hole with rounded ends) on the breaking strength of human femora. They found that an oblong hole with rounded ends afforded the greatest residual strength.²⁵ They also found that increasing the width of the hole caused a significant reduction in strength, but increasing the length did not.²⁵ Therefore, when the biopsy must be taken from the bone, a small circular hole should be made so that only minimal stress-risers are created. If a larger window is needed, an oblong window should be made (Figure 2.9). (3) Obtain

enough tissue. Always send a specimen for frozen section or touch-prep to verify the presence of representative tumor material in the specimen. For needle biopsies, cytopathologic evaluation has to confirm the presence of viable tumor cells. If pathologic evaluation is negative or questionable, repeat the biopsy. (4) As a general rule, culture what you biopsy and biopsy what you culture. (5) Use meticulous hemostasis. Any hematoma around a tumor should be considered contaminated. Large hematoma may dissect the soft and subcutaneous tissues and contaminate the entire extremity, making limb-sparing surgery impossible. A tourniquet is rarely indicated for an open biopsy, because bleeding vessels cannot be observed and adequate hemostasis is hard to achieve. If a tourniquet is used, the limb should not be exsanguinated by wrapping with an Esmarch bandage, because this may force tumor cells to the proximal aspect of the extremity and into the bloodstream. To allow hemostasis, the tourniquet must be removed before wound closure. (6) Use drains if necessary. The port of entry has to be in proximity and continuation with the skin incision, not to its sides (Figure 2.10). The drain path is considered contaminated and has to be excised with the surgical specimen. Guidelines regarding the excision of the draining tract therefore are similar to those that apply to the biopsy tract.

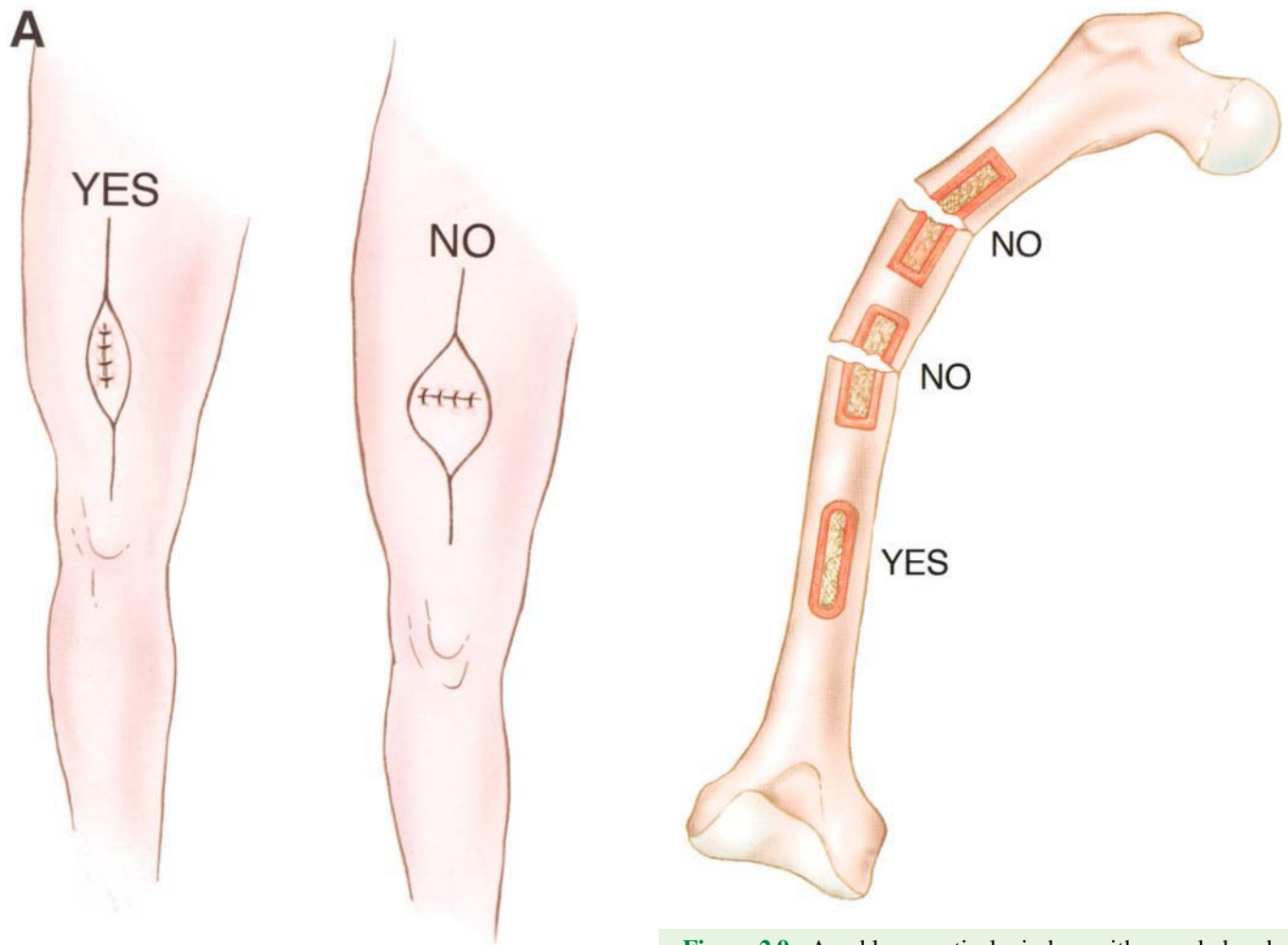


Figure 2.9 An oblong cortical window with rounded ends affords the greatest residual strength and is recommended for biopsy of purely intraosseous lesions.

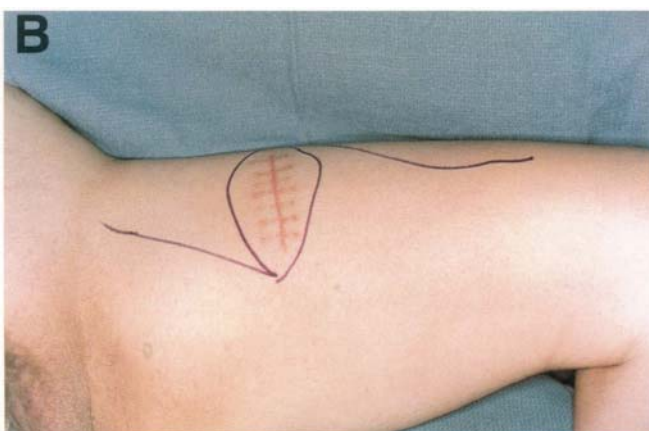


Figure 2.8 (A) The smallest longitudinal incision that allows an adequate specimen to be obtained should be used. A transverse biopsy incision requires a wider resection of soft tissues at the time of the definitive surgery. (B) Horizontal biopsy incision over a high-grade soft-tissue sarcoma of the thigh. Definitive surgery had to be modified to include the biopsy incision.

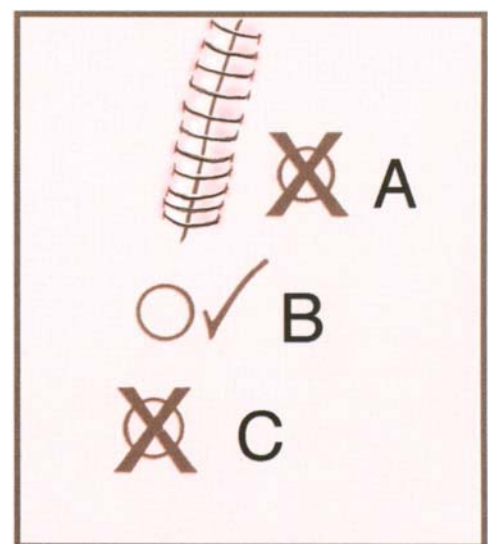


Figure 2.10 A drain has to be positioned in proximity to and along the site for planned incision of the definitive procedure.

SUMMARY

Accurate diagnosis of a musculoskeletal tumor is based on these factors: clinical presentation, results of radiologic studies, and pathologic evaluation. The importance of careful planning and performance of a

biopsy cannot be overemphasized because an error may have a negative impact on survival, impede a proper diagnosis, and compromise the ability to perform limb-sparing surgery. Core needle biopsies, performed under CT guidance when indicated, are recommended.

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3

The Role of Chemotherapy in the Treatment of Bone and Soft-tissue Sarcomas

Dennis Priebat and Martin Malawer

OVERVIEW

Sarcomas are rare, mesenchymal tumors of the soft tissue and bone that exhibit a marked heterogeneity in their clinical presentation, biologic behavior, and histologic features. Approximately 10,400 new cases are diagnosed annually, 7800 of which arise from the soft tissues (50–60% of which involve the extremities) and 2600 from bones.¹ Although the incidence of extremity sarcomas is similar to that of Hodgkin's disease, they are responsible for more than twice as many deaths each year. Major advances in the treatment of these tumors have been limited by an inability to accumulate sufficient numbers of similar patients to perform prospective randomized clinical trials with results that can achieve statistical significance.

Until the 1970s, surgery and/or radiation therapy was the accepted method for the primary management of most soft-tissue and bone sarcomas of the extremities. However, surgery alone, especially wide resection, was associated with a high incidence of local recurrences. Even when local control was achieved, more than 50% of patients with soft-tissue sarcoma and 80% of patients with skeletal sarcoma (osteogenic and Ewing's sarcoma) eventually developed distant metastases and died, usually within 2 years.^{2–11} Systemic chemotherapy was subsequently found to exhibit reproducible anti-tumor effects against these neoplasms. Initially used only in the treatment of metastatic disease, this was later used as a part of combined-modality therapy in the adjuvant (postoperative) setting, and then as preoperative (neoadjuvant, induction) therapy in an attempt to preserve limb function and/or increase long-term survival.^{2–11} The routes of chemotherapy administration have included intravenous (IV) bolus, continuous IV infusion, and local (regional) drug delivery directly to the tumor via a feeding artery.¹²

SOFT-TISSUE SARCOMA

Despite the development of successful therapeutic modalities for local tumor control (e.g., limb-sparing surgery and radiation therapy), 40–50% of patients, particularly those with high-grade, large, deep tumors, will have local recurrences and die from metastases that were not apparent at presentation.³ An additional 10% of patients will have metastases (usually lung) at the time of initial diagnosis. Consequentially, chemotherapy was used initially to treat metastatic disease and, more recently, in an attempt to increase survival after local treatment and to also maximize the number of candidates for limb-sparing surgery.^{13,14}

Chemotherapy Development

Only two single agents, Adriamycin and ifosfamide, have shown a reproducible response that is greater than 20% for soft-tissue sarcomas.¹⁵ The largest experience with single-agent chemotherapy in this disease is with Adriamycin. A steep dose–response relationship has been found for Adriamycin. This was first demonstrated in the Southwest Oncology Group (SWOG) study in the 1970s, in which a dose of 75 mg/m² given every 3 weeks was shown to have a superior response rate to doses of 60 mg/m² and 45 mg/m².¹⁶ Further evidence of a dose response has come from other studies of Adriamycin administered alone, as well as in conjunction with ifosfamide.^{17,18} Unfortunately, Adriamycin also has an associated dose-limiting cardiotoxicity. The cardiotoxicity has been reduced without altering the drug's effectiveness by administering it as a continuous IV infusion over 72–96 h via a central venous catheter rather than by bolus dosing.^{19,20} To obtain an optimal response it appears to be important to achieve a dose intensity of at least 70 mg/m² every 3 weeks.¹⁵

Analogues of Adriamycin have been developed in an attempt to reduce the potential for cardiotoxicity that exists at higher cumulative doses. Epirubicin has been the most extensively studied. The EORTC Sarcoma Group compared equitoxic doses of Adriamycin 75 mg/m² and epirubicin 150 mg/m² (given as a single bolus or fractioned over 3 days).²¹ An overall response rate of 18% was obtained. No difference was seen between the three study arms; however, myelosuppression was greater for epirubicin than for Adriamycin. The incidence of cardiotoxicity was similar for both agents. Unfortunately, none of the currently available anthracycline analogues show any advantage over Adriamycin for patients with soft-tissue sarcomas, and early studies of the new liposomal Adriamycin derivatives have shown variable activity.²²

Alkylating agents have also been studied extensively, but only ifosfamide has shown activity equivalent to that of Adriamycin.¹⁵ Prior to the availability of ifosfamide, cyclophosphamide was used widely as a component of the CyVADIC regimen, largely on the basis of its reported activity in pediatric sarcomas (especially rhabdomyosarcoma). Since the introduction of ifosfamide there has been considerable debate over its activity compared with that of cyclophosphamide. In the 1980s the EORTC performed a randomized trial comparing a 24-h continuous infusion of cyclophosphamide 1.5 g/m² versus ifosfamide 5 g/m² (chosen to produce a comparable degree of myelosuppression).²³ The response rate for ifosfamide in previously untreated patients with sarcoma was 25% versus 13% for cyclophosphamide.

In addition, ifosfamide showed activity in previously treated patients and in patients who were resistant to cyclophosphamide. There were no responses observed in patients crossed over to cyclophosphamide, indicating an incomplete cross-resistance between the two agents. Leukopenia was much less common in patients who received ifosfamide, suggesting that further dose escalation would be possible.

Both the dosage and scheduling appear to be important factors for the use of ifosfamide in soft-tissue sarcomas. Doses of less than or equal to 8 g/m² demonstrated clinical activity in numerous studies in the 1980s.²⁴ But it was only in the 1990s that a dose–response activity relationship was recognized and fully evaluated.^{25,26} There appeared to be further anti-tumor activity of high-dose ifosfamide (12–14 g/m²) in patients who did not respond to lower doses or who relapsed after standard dose ifosfamide-containing regimens.^{24,26–28} Several dose-intensified studies have shown higher clinical response rates than conventional dose regimens. When ifosfamide is used as a single-agent therapy, several experts recommend that a dose of ≥ 10 g/m² be the minimum needed to obtain an optimal response for patients with soft-tissue sarcomas. It was only with the availability of mesna (M), which protects against urothelial toxicity (i.e., hemorrhagic cystitis), that the clinical use of this agent has become practical. The scheduling of ifosfamide also appears to be important. Studies by Antman *et al.* and Patel *et al.* have suggested that a 2–4 h IV bolus schedule appears to have approximately twice the response rate as a continuous IV infusion.^{26,29} Results of a recent EORTC randomized trial that compared two different dose schedules of ifosfamide (5 g/m² over 24 h vs. 3 g/m² over 4 h, day 1–3), demonstrated an advantage for the IV bolus intensive regimen in terms of response (10% vs. 25%).³⁰ This same group also evaluated ifosfamide given at 12 g/m² as a 72-h continuous IV infusion q 4 weeks,

which yielded an overall response rate of only 14%.³¹

Ifosfamide has been shown to have significant activity against synovial cell sarcoma.²⁷ With the availability of mesna, it is much safer to use, but it still has dose-limiting myelosuppression, renal and central nervous system (CNS) toxicity.³² Vigorous hydration with electrolytes and bicarbonate/acetate must be utilized to prevent severe metabolic acidosis and reduce the risk of significant neurotoxicity. CNS toxicity usually presents as a metabolic encephalopathy that may include confusion, blurred vision, mutism, auditory or visual paranoid hallucinations, seizures, and rarely, coma.²⁹ The exact mechanism for this toxicity is not known, but it may be related to the accumulation of chloroacetaldehyde, one of ifosfamide's metabolites. Patients who are particularly prone to renal and CNS toxicity include those with a poor performance status, low serum albumin level (< 3 g/dl), renal dysfunction (as indicated by a prior nephrectomy, clinical or subclinical renal tubular dysfunction, or previous treatment with cisplatin), and bulky pelvic disease, as well as those over the age of 65.³²

Neurotoxicity is usually self-limited. Methylene blue (50 mg IV) and diazepam (5 mg IV) have been reported to rapidly reverse the encephalopathy; however, methylene blue should not be given to patients who are glucose-6-phosphate dehydrogenase (G6PD)-deficient.^{33,34} Both these agents can be given prophylactically in subsequent cycles in order to prevent neurotoxicity (i.e., methylene blue 65 mg tablets qid). Hematologic toxicity in terms of myelosuppression has been ameliorated through the use of the hematopoietic growth factors G or GM-CSF, but patients still can develop dose-limiting thrombocytopenia.³⁵ This may be better controlled in the future with the use of new thrombopoietin agents.

Dacarbazine (DTIC) has also been used extensively for soft-tissue sarcomas, but it has a response rate under 20% as a single agent.¹⁵ Emesis, a major side-effect, can be reduced when the drug is given as a continuous IV infusion. Its use with ifosfamide and Adriamycin in the MAID regimen has been questioned since it may contribute to increased toxicity with minimal additional efficacy. There is some evidence that DTIC has particular activity against non-gastrointestinal leiomyosarcoma.³⁶

Most other agents have had disappointingly low response rates for soft-tissue sarcoma. Methotrexate has minimal activity, and 5-fluorouracil and its derivatives are inactive.^{17,18} Vincristine, which was initially incorporated in combination regimens because of its activity in pediatric soft-tissue sarcomas, has a low response rate. The newer taxanes have minimal, if any, activity.^{37,38} A recent study shows a synergistic effect for cisplatin when given with epirubicin, and several

preliminary reports suggest that gemcitabine may also have activity.^{39,40}

Combination Therapy in the Treatment of Advanced Disease

Given the modest results of single-agent chemotherapy in the treatment of soft-tissue sarcomas, several combination chemotherapy regimens have been explored.^{15,18} There is still controversy as to whether single-agent Adriamycin or a multi-agent regimen that includes Adriamycin is better for the treatment of advanced disease.^{41,42} In the 1980s, Adriamycin (A) and DTIC (D) was the most commonly recommended combination regimen. ECOG and GOG studies showed higher response rates for the AD combination, but because there was no survival advantage and greater gastrointestinal toxicity for AD, both groups concluded that Adriamycin alone was preferable.^{15,18} In a SWOG study, AD had reduced toxicity (i.e., cardiac, nausea, and vomiting) comparing a 96-h IV infusion to bolus, and still equivalent tumor activity and survival.¹⁹ Several other studies have shown no advantage for adding other agents (i.e., cytoxan, vincristine, actinomycin-D).¹⁵ It was felt that these agents simply reduced the dosage of Adriamycin that could be safely used.

Based on its activity in refractory and relapsed soft-tissue sarcoma, ifosfamide with mesna has been studied in combination with Adriamycin and Adriamycin/DTIC. In the late 1980s the MAID regimen was pioneered at the Dana Farber Cancer Institute (DFCI). MAID was a logical modification of the CyVADIC regimen; it eliminated the inactive vincristine and replaced cyclophosphamide with ifosfamide.⁴³ Studies from the DFCI using MAID reported a response rate of approximately 50% (10% complete response). In Europe, substitution of epirubicin for Adriamycin yielded similar results.^{15,17,18} Although the MAID regimen has been used extensively in the 1990s for the treatment of soft-tissue sarcoma, it is a highly toxic therapy with severe life-threatening myelosuppression. Furthermore, adjusting the dosage of the regimen components has not significantly decreased toxicity or improved efficacy.

The effect of adding DTIC to this regimen has been unclear, since its single-agent activity is less than that of the other two components and it may be increasing toxicity without improving response. There have been three randomized trials of Adriamycin (A) with or without ifosfamide (I); EORTC, ISSG (Intergroup), and ECOG (Table 3.1).⁴⁴⁻⁴⁶ The ECOG and ISSG studies both showed a significant increase in response rate for the AI regimen. However, in all three studies there was significantly more myelosuppression (including fatal

Table 3.1 Combination chemotherapy regimens containing Adriamycin and ifosfamide for soft-tissue sarcomas - randomized studies

Study	Regimen	No. of patients	%CR	% OR	Median survival (months)
ISSG	A (60 mg/m ²), D (1 g/m ²)	170	2	17	13
Antman	A (60 mg/m ²), D (1 g/m ²) I (7.5 g/m ² → 6.0 g/m ²)	166	4	32	12
				<i>p</i> = 0.005	<i>p</i> = NS
EORTC	A (75 mg/m ²)	240	4	23	12
Santoro	A (50 mg/m ²), I (5 g/m ²)	231	6	28	12
	ACDV-A (50 mg/m ²)	134	8	28	13
				<i>p</i> = NS	<i>p</i> = NS
ECOG	A (80 mg/m ²)	90	2	20	9
Edmonson	A (60 mg/m ²) I (7.5 g/m ²)	88	3	34	12
	A (40 mg/m ²) P (60 mg/m ²), Mi (8 mg/m ²)	84	7	32	9
				<i>p</i> = 0.03	<i>p</i> = NS
EORTC	A (75 mg/m ²), I (5 g/m ²)	104	10	45	15
Steward	+GM-CSF (molgramostim)	134			
EORTC	A (50 mg/m ²), I (5 g/m ²)	134	3	20	
Tursz				<i>p</i> = NS	
	A (75 mg/m ²), I (5 g/m ²) +GM-CSF (sargramostim)	128	3	21	

I = ifosfamide, C = cytoxan, A = Adriamycin, D = DTIC, V = vincristine, P = cisplatin, Mi = mitomycin C, NS = not significant, CR = complete response; OR = objective response

sepsis) for AI, with no significant advantage in survival. Furthermore, in the middle of the ISSG trial, the MAID group protocol was amended to reduce the starting dose of ifosfamide from 7.5 g to 6 g/m².⁴⁴ There was also a significant decrease in the delivered dose of Adriamycin by the fourth cycle (from 60 to 51 mg/m²). Patients with low- to intermediate-grade tumors responded less frequently to MAID (18%) than to AD (29%). A univariate analysis demonstrated a significant survival advantage for the two-drug arm AD in patients greater than 50 years old and those with low- to intermediate-grade tumors. This advantage for AD has been hypothesized to be due to the lower dose intensity of Adriamycin in the three-drug arm and to the fact that patients who failed on the AD arm subsequently received ifosfamide, which provided a secondary benefit.

The focus of research has now shifted to the two most active chemotherapy agents Adriamycin and ifosfamide, with dose intensification utilizing hematopoietic growth factors.^{41,47-50} This approach is based on the hypothesis that their previous use at less than full doses in combination regimens with other agents (i.e., the

MAID regimen) may have compromised their activity. An EORTC study utilizing GM-CSF support with high-dose Adriamycin showed the highest response rate (45%; 10% CR) so far seen by this cooperative group for advanced soft-tissue sarcomas (10% above their standard AI regimen).³⁵ This was followed by a larger phase III randomized trial comparing this higher-dose Adriamycin regimen with their conventional dose regimen (Adriamycin 50 mg/m² and ifosfamide 5 g/m²).^{41,51} The response rates, progression free interval, and overall survival were found to be similar for the two study arms. Unfortunately, some have concluded from these results that the activities of dose-intensified Adriamycin and ifosfamide regimens are disappointing. However, the dose and scheduling of ifosfamide in this trial was suboptimal. Furthermore, the predominant histologic subtype of the patients was leiomyosarcoma (38%), which is inherently more chemotherapy-resistant. Therefore, with a smaller overall number of possible chemotherapy-responsive sarcoma patients, the chance of detecting a small but significant difference between the two treatment arms was markedly reduced.

Recently, Patel and colleagues at M.D. Anderson Cancer Center (MDACC) escalated the doses of Adriamycin and ifosfamide further and have obtained the highest reported response rates to date.^{47,48} They conducted two pilot studies to evaluate the feasibility and activity of Adriamycin at either 75 mg/m² or 90 mg/m² combined with ifosfamide at 10 g/m² (2 g/m² for 5 days) with G-CSF support. The overall objective response rate in 79 evaluable patients was 65%. There was no further benefit in improved response with the higher Adriamycin dose arm, but about 50% of patients experienced Grade 3–4 thrombocytopenia within the first two cycles, and virtually all patients by cycle three. Results of time to progression and survival analysis are still pending. This higher dose therapy is felt to be feasible only for selected patients (i.e., age less than 65, ECOG performance status 0–1, no prior chemotherapy, and radiation therapy to less than 20% of the bone marrow). Bokemeyer *et al.* kept the dose of Adriamycin at 75 mg/m² and escalated the doses of ifosfamide to 14 g/m² with G-CSF and peripheral blood stem cell support.⁴⁹ This resulted in a 50% response rate with 22% complete responses.

These preliminary data appear to reflect a real improvement over previous experience with the MAID regimen. At present, the highest reported response rate for soft-tissue sarcoma is with a high-dose Adriamycin–ifosfamide regimen; however, it is associated with severe (although short-lived) myelosuppression, including significant cumulative thrombocytopenia. Whether the improved response rate will translate into a significant survival advantage is not yet known.⁴¹ New growth factors (e.g., thrombopoietin) could further reduce the hematologic toxicity and enhance dose intensity. An improved response rate may be more important for early-stage disease (i.e., in the neoadjuvant or adjuvant setting) for young, good-performance status patients with a high-grade, borderline resectable lesion, or patients with pulmonary metastases who are borderline candidates for metastectomy. A significant response could facilitate subsequent surgery and/or radiation therapy, and render the patient disease-free.

For palliation, particularly in older or poor-performance status patients and in those with low- to intermediate-grade tumors, Adriamycin and Adriamycin/DTIC regimens seem preferable. Toxicity can be reduced by giving this regimen as a continuous IV infusion.

Adjuvant Chemotherapy

Although the role of adjuvant chemotherapy is well established in the treatment of rhabdomyosarcoma, osteosarcoma, and Ewing's sarcoma, its use in soft-tissue sarcomas remains controversial and unre-

solved.^{52–56} Published articles range from retrospective reviews of outcome at single institutions, to prospective nonrandomized studies, to formal randomized trials.

Most of these studies have enrolled few patients (less than 100); have used different patient inclusion criteria and had an imbalance between the two arms with respect to pathologic grade, histologic subtype, and anatomic site; or utilized different drugs, doses, and schedules (some with suboptimal delivery and a delayed start). Several have an extremely short follow-up period, while others included patients with good risk factors (i.e. small, [less than 5 cm], low-grade tumors). For these reasons it is hard to draw meaningful conclusions concerning the validity of their results.

The resection of pulmonary metastases and the use of preoperative chemotherapy may also affect overall survival. Furthermore, it is difficult to detect small, but potentially clinically important, differences in survival, when only moderately effective chemotherapy regimens are used. Several single-arm studies show adjuvant chemotherapy to be beneficial when compared with historical controls; however, in nearly all the prospective randomized trials with an observation arm, there is no difference in overall survival. Both the treated and observation (control) arms do better than previous historical controls. Most studies show a trend toward longer disease-free survival but no significant increase in overall survival.

Twelve randomized studies have used the most active agent, Adriamycin, either alone or in combination (Table 3.2). Two (Fond Bergonie-Bordeaux and the Rizzoli Institute) showed a significant overall survival advantage for the patients receiving adjuvant chemotherapy; however, both of these studies were quite small. The remainder of these studies showed no increase in overall survival. None of the studies included ifosfamide, either alone or in combination.

A 5-year follow-up of a National Cancer Institute (NCI) study utilizing cytoxan, Adriamycin (total dose 530 mg/m²), and methotrexate (CAM) showed a significant increase in disease-free and overall survival rates for the subset of patients with extremity sarcomas. However, at re-evaluation 2 years later (7.1 years median follow-up), overall survival was no longer significantly better for patients who had received adjuvant chemotherapy.⁵⁷ There was no significant benefit of chemotherapy for truncal and head and neck sarcomas. In patients with retroperitoneal disease, the control group fared better than the chemotherapy group. Cardiotoxicity, for the chemotherapy arm, was significant (14% congestive heart failure and greater than 50% abnormal MUGA scans). In the NCI's most recent study, with reduced total Adriamycin (350 mg/m²), the

Table 3.2 Randomized adjuvant trials in soft-tissue sarcomas

Study	Regimen	No. of patients	% DFS		% OS	
			–	+	–	+
EORTC	ACVD	468	61	61	68	74
Extremities		233	52	67	74	79
FondBergonie	ACVD	59	16	57 $p < 0.01$	53	87 $p < 0.01$
Extremities		36	NA	NA	NA	NA
Mayo Clinic	AVDAd	61	68	65	70	70
Extremities		48	67	88 $p = 0.08$	83	63
MDAnderson	ACVAd	47	83	76	NA	NA
Extremities		43	35	54 $p < 0.05$	46	65
NCI	ACM	31	49	77 $p = 0.075$	58	68
Nonextremity/nonretroperitoneal		22	47	92 $p < 0.01$	61	82
Trunk		15	NA	NA	100	47 $p = 0.06 \uparrow$
Retroperitoneal		67	54	75 $p < 0.05$	60	82
Extremities						
Scandinavian	A	181	56	62	70	75
Extremities		155	NA	NS	NS	NS
Pooled DFCI/MGH, ISSG, ECOG	A	168	53	66	65	68
Extremities		72	64	79	70	79
GOG	A	156	47	59	52	60
UCLA	A	119	54	56	74	78
Extremities						
Rizzoli	A	77	45	73 $p < 0.05$	70	91 $p < 0.05$
Extremities						

DFS = disease free survival, OS = overall survival, (–) = observation, (+) = chemotherapy; NS = not significant, A = Adriamycin, C = cyclophosphamide, V = vincristine, D = dacarbazine, Ad = actinomycin D, M = methotrexate.

Modified from Mazanet R, Antman KH. Sarcomas of soft tissue and bone. Cancer. 1991;68:463–73.

disease-free and overall survival was found to be similar to that of the initial regimen, but cardiotoxicity was reduced.

An updated report by the Rizzoli Institute at greater than 10 years median follow-up showed a significant increase in disease-free survival ($p = 0.015$) and overall survival ($p = 0.04$) for adjuvant chemotherapy.⁵⁸ This study has been criticized because of an imbalance of large pelvic and thigh tumors between the control and chemotherapy groups.

An update of the large, randomized trial from the EORTC (median follow-up 80 months) reconfirmed that there was no difference in overall survival for CyVADIC adjuvant chemotherapy (63% versus 56%, $p = 0.64$).⁵⁹ Rates of relapse-free survival (56% versus 43%, $p = 0.007$) and local recurrence (17% versus 31%, $p = 0.004$) were significantly reduced. The reduction in local recurrence was apparent only for head, neck, and

trunk sarcomas. Interestingly, only 68% of entered patients (317 of 468) were found to be eligible, and chemotherapy was not started for a median of 6 weeks after surgery (maximum 13 weeks).

There have been four published meta-analyses of the randomized adjuvant studies utilizing Adriamycin-based chemotherapy for soft-tissue sarcomas.^{53,56} Three analyzed only the published data and showed a significant advantage in disease-free and overall survival rates for patients receiving adjuvant chemotherapy.⁵³ These meta-analyses have been criticized because the data are abstracted from narrative text and tables instead of from the raw data, and they did not include the most recent results from the EORTC and Rizzoli Institute. They also suffer from a number of other possible flaws (i.e., biases due to the exclusion of unpublished trials; inappropriate postrandomization patient exclusions; variable follow-up time; and a fixed

time-point analysis with deferring definitions of end points), all of which could contribute to overestimates of the treatment effect and significance.

Tierney *et al.* of the MRC Cancer Trials Office and the Sarcoma Meta-Analysis Collaboration, published an individual patient data meta-analysis (IPD-MA) of updated outcomes of 1568 patients from 14 randomized trials of Adriamycin-based adjuvant chemotherapy versus observation control (Table 3.3).⁵⁶ The median follow-up period was 9.4 years. Soft-tissue sarcomas of all sites, sizes, grades, and histologies were included. Only 59% of the histologic subtypes and 25% of the grades had been reviewed at the time of its publication. This IPD-MA showed a significant improvement for adjuvant chemotherapy with respect to time to recurrence (local and distant) and disease-free survival, but only a trend for benefit in overall survival. Of further interest, for the subset of patients with extremity soft-tissue sarcoma ($n = 886$), there was a significant absolute benefit in overall survival at 10 years (7%, $p = 0.029$). This finding must still be viewed cautiously since it was not included as part of the initial randomization and analysis, and there can be inherent dangers in the later evaluation of subsets. In addition, this IPD-MA may not be fully relevant for present medical practice, because it did not include adjuvant studies containing ifosfamide or using hematopoietic growth factors to maintain dose intensity.

Recently, Frustaci *et al.* reported on the Italian Cooperative Soft-Tissue Sarcoma Group's randomized adjuvant trial of 104 patients with high-risk (i.e. high-grade, deep, and greater than 5 cm) extremity soft-tissue sarcomas utilizing high doses of epirubicin and ifosfamide with G-CSF support.^{60,61} At a median follow-up of 24 months (range 5–57 months), there was a significant difference in favor of the chemotherapy arm

for both disease-free ($p = 0.001$) and overall ($p = 0.005$) survival. At interim analysis, after only half of the planned number of patients had been randomized, the investigators decided to stop accrual, even though follow-up was short. No evaluation of toxicity was reported. Nonetheless, these data, the first from a randomized trial evaluating aggressive chemotherapy with an ifosfamide-containing adjuvant regimen, are encouraging. Follow-up is ongoing, and the study will need to be confirmed with a larger number of patients by another multi-institutional group.

Since the survival of patients with high-grade extremity soft-tissue sarcomas is already 50–70% at several centers, it will be increasingly difficult to show a statistically significant difference in randomized adjuvant trials.⁶² More patients will be needed to show small differences in survival. Patients with low-grade sarcomas should not be given adjuvant chemotherapy, because of their inherently low rate of metastatic spread and excellent prognosis. In addition, small (less than 5 cm), superficial, high-grade primary extremity sarcomas should not be included, since recent studies also suggest that these patients have an excellent survival.^{5,63} Despite their limitations the IPD-MA and the Italian study indicate that adjuvant therapy is beneficial for select patients with extremity soft-tissue sarcoma. Future randomized trials should include only patients at high risk for metastases (i.e., large, high-grade, deep-seated lesions) with a reasonable likelihood of local control (radical resection or resection with uninvolved margins and radiotherapy). The recent NCCN Practice Guidelines recommend considering adjuvant chemotherapy with an aggressively dosed ifosfamide/Adriamycin regimen for patients with Stage IIB or IIIB extremity sarcomas who have undergone optimal resection, with or without radiation therapy.⁵

Table 3.3 Adjuvant chemotherapy of adult soft-tissue sarcoma: meta-analysis of individualized patient data

	Absolute benefit (at 10 years)		Hazard ratio	p-Value
	–	+		
Recurrence-free interval				
Local	6%	(75 → 81%)	0.73	0.016
Distant	10%	(60 → 70%)	0.70	0.0003
Survival				
RFS	10%	(45 → 55%)	0.75	0.0001
OS	4%	(50 → 54%)	0.89	0.12
	7%	(extremity)	0.80	0.029

Tierney JF. Lancet. 1997;350:1647–54.

(–) = Observation, (+) = adjuvant chemotherapy.

RFS = recurrence-free survival; OS = overall survival

Neoadjuvant Chemotherapy

Neoadjuvant (induction) chemotherapy for soft-tissue sarcomas of the extremities evolved as a result of studies initially performed for osteogenic sarcoma. Routes of administration have included IV bolus, continuous IV infusion, and intra-arterial regional therapy, with or without concomitant radiation therapy.^{12,64} They have also included isolated limb perfusion.⁶⁵ Neoadjuvant therapy has primarily been utilized for patients with large primary or recurrent sarcomas, usually with the goal of permitting a limb-sparing operation in patients in whom amputation may otherwise have been necessary or for converting a marginally resectable tumor to one that can be adequately resected with preservation of extremity function. Although initial local tumor control and limb-salvage rates appear very good, most studies have enrolled only small numbers of patients and have a short follow-up. Therefore, the effect of neoadjuvant therapy on disease-free and overall survival rates is not fully known. There have been no prospective randomized trials comparing preoperative and postoperative chemotherapy for patients with soft-tissue sarcoma. Nevertheless, patients with large, deep-seated, high-grade lesions of the extremities are a high-risk group that is an optimal target population for investigating the effectiveness of multimodality treatment strategies.

There have been several representative early reports of the use of IV preoperative chemotherapy for extremity sarcomas with Adriamycin-based regimens. Pezzi *et al.* from M.D. Anderson summarized a 7-year experience (1979–1985) with preoperative Adriamycin-based systemic therapy (an average of four cycles), with or without radiation therapy, in 46 patients with large tumors (median 10.6 cm).⁶⁶ The clinical response rate was 23%. Limb-sparing surgery could be performed in 67% of patients, but the local recurrence rate was 34%, and overall survival (median of 28 months follow-up) was 62%. In a study by Casper *et al.* from MSKCC, which entailed administration of two cycles of preoperative CyVADIC to 22 patients with large extremity soft-tissue sarcomas (median 10 cm), there was only one partial clinical response, and just 10% of patients had greater than 90% tumor necrosis.⁶⁷ Median 3-year disease-free survival was 36%, overall survival at 3 years was 45%. There was no survival advantage between this study group and a historical control group of patients with surgery alone or surgery plus postoperative Adriamycin. Possible explanations for the lower response rate could have been a lower Adriamycin dose (60 mg/m²), as well as administration of fewer cycles of preoperative chemotherapy.

Pisters *et al.* reported on 76 patients with large high-grade extremity sarcomas treated at M.D. Anderson

between 1986 and 1990 who received a median of three preoperative cycles of IV Adriamycin/DTIC (+/–) cyclophosphamide or other Adriamycin-based regimens.⁶⁸ Limb-sparing surgery was able to be performed in 91% of these patients. Five-year actuarial disease-free survival was 46%, and overall survival was 54% (median follow-up 85 months).

Much of the pioneering work utilizing preoperative chemotherapy for extremity soft-tissue sarcomas has been conducted by the University of California at Los Angeles (UCLA) group.^{69,70} Their experience entails five sequential trials over a 20-year period (Table 3.4). They initially utilized a preoperative continuous infusion of intra-arterial Adriamycin 90 mg (30 mg/day for 3 days), a suboptimal dose, followed by varying amounts of preoperative radiation therapy in three sequential studies. Utilizing 3500 cGy produced a low local recurrence rate, but a high incidence (25%) of complications. When the dosage was decreased to 1750 cGy the complication rate (including bone fractures) decreased, but the local recurrence rate increased. The protocol was again modified in 1984 to incorporate an intermediate radiation dose of 2800 cGy (350 cGy/day for 8 days). In addition, the preoperative Adriamycin dose was randomized to be given either as an intra-arterial or IV infusion. Ninety-nine percent of patients were able to undergo a limb-sparing procedure, and the local recurrence rate was only 8%. Complications occurred in 14% of patients, which was less than with the higher dose of radiation. At a median follow-up of 36 months there was no significant difference between the IV and the intra-arterial groups in the limb salvage, local recurrence or complication rate; percentage of histological necrosis; or disease-free survival. This study has been cited by some as evidence for the lack of efficacy of intra-arterial chemotherapy. However, the dosage of Adriamycin was suboptimal, and at the time of initial randomization the two treatment groups were not stratified for tumor size and grade. The intra-arterial group contained a greater percentage of patients with large (>10 cm), high-grade tumors. Several other investigators have attempted to reproduce the UCLA group results using intra-arterial Adriamycin.¹² The results appear to be similar, with a fairly high complication rate. On the basis of these findings it was concluded that Adriamycin is not the proper drug for intra-arterial use because of problems with musculoskeletal necrosis.

The UCLA group then investigated the use of intravenous cisplatin 120 mg/m² over 4 h with Adriamycin 60 mg/m² given via continuous infusion over 48 h followed by radiation 2800 cGy. The limb-sparing and local recurrence rates remained about the same, but the complication rate was reduced.

Table 3.4 UCLA – neoadjuvant chemoradiation protocols for soft-tissue sarcoma

Protocol	Years	Chemotherapy	Radiation dose (cGy)	Percentage median tumor necrosis	Percentage pathologic CR necrosis	Percentage local recurrence	Percentage overall survival grade III tumors
Pilot	1973	ADR 90 mg IA over 3 d	3500	–	–	–	–
1	1974–80	ADR 90 mg IA over 3 d	3500	70	12	9	56
2	1981–84	ADR 90 mg IA over 3 d	1750	45	4	20	61
3	1984–87	ADR 90 mg IA or IV over 3 d	2800	60	6	14	70
4	1987–90	CDP 120 mg/m ² IV over 4 h ADR 60 mg/m ² IV over 48 h (two cycles)	2800	70	15	12	71
5	1990–93	IFOS 14 g/m ² IV over 7 d CDP 120 mg/m ² IV over 4 h ADR 75 mg/m ² IV over 48 h (one cycle)	2800	98	34	2	85

Adr = Adriamycin; IFOS = ifosfamide; CDP = cisplatin; h = hours; d = days; IV = intravenous; IA = intraarterial

In an attempt to augment the pathologic complete response rate, the UCLA group next added two cycles of high-dose ifosfamide at 14 g/m² to the neoadjuvant chemotherapy and radiation regimen.⁶⁹ Radiation (2800 cGy) was given during the second cycle of ifosfamide, and this was then followed by one cycle of cisplatin/Adriamycin. When retrospectively compared with the previous sequential trials at UCLA, this regimen resulted in a markedly improved complete pathologic response of 34% vs. 7.4%, the combined complete response rate for all prior trials. At a median follow-up of 27 months, local failure was 2% and overall survival was 87%, with 98% of patients undergoing a limb-salvage procedure. These results are impressive despite the fact that this is fairly toxic, requiring significant replacement of blood components for cytopenias and hospitalizations for febrile neutropenia. Whether, with longer follow-up, the improved complete pathologic response rate will translate into an improved overall survival (as hypothesized) is not yet known.

Investigators at MGH have combined three preoperative cycles of a MAID-type chemotherapy with radiation (4400 cGy) in a neoadjuvant regimen for large (>8 cm), high-grade extremity soft-tissue sarcomas.⁷¹ At a short median follow-up of 13 months, local control was 100%, disease-free survival 84%, and overall survival 93%. When compared with a historically matched control group from the same institution, the results of this study group were significantly better.

Based on these data, a Phase II Intergroup (ECOG and RTOG) study is now seeking to confirm these results in a multi-institutional setting.

Our group evaluated a short course of combination regional/systemic chemotherapy consisting of two preoperative cycles of intra-arterial cisplatin (120 mg/m² over 2 h) and continuous IV infusion Adriamycin (60 mg/m² over 72 h) in 24 patients with large, high-grade, unresectable/borderline resectable soft-tissue sarcomas of the extremities.⁷² This regimen was utilized based on its known activity in osteogenic sarcoma, and on the fact that, although cisplatin has low-single agent activity for soft-tissue sarcoma, it appears to have a synergistic effect when given with Adriamycin. With this neoadjuvant regimen, 92% of patients were able to undergo limb-sparing surgery, and the local control rate was 87%. After surgery, four adjuvant cycles of IV cisplatin/Adriamycin were given. Postoperative radiation was used only for patients with positive margins or massive contamination from previous inadequate surgery. At a median follow-up of 76 months, disease-free survival was 66% and overall survival 83%. No patient developed major cardiac or renal dysfunction; however, 29% of these patients developed significant peripheral neuropathy that was probably due to cumulative cisplatin.

A new protocol, initiated in 1995, adds one cycle of IV ifosfamide at 9 g/m² (2.25 g/m² per day for 4 days) combined with Adriamycin to the preoperative regimen (Figure 3.1). The dose of Adriamycin for all cycles has

been increased to 75 mg/m^2 , with G-CSF support afterwards. Postoperatively, three cycles of ifosfamide and Adriamycin at the same dose are given.⁷³ Thus far, the incidence of severe peripheral neuropathy has been significantly reduced; however, it is too early to determine whether this regimen will be superior in terms of local control, disease-free, and overall survival.

Hyperthermic isolated limb perfusion with melphalan and tumor necrosis factor has been used in patients with large soft-tissue extremity sarcomas that are close to bone, nerve, and/or blood vessels and in whom amputation would otherwise be necessary (see Chapter 4). A high limb-salvage rate ($>80\%$), has been reported.^{65,74} This is, however, a localized treatment when used alone, and there has been no control of or reduction in the recurrence of systemic disease.

In conclusion, neoadjuvant chemotherapy for large, high-grade soft-tissue sarcomas of the extremities is feasible and associated with good local control and survival. Limb-sparing surgery is possible in the overwhelming majority of these patients. More aggressive regimens appear to reduce local recurrence and result in a high complete pathologic response rate. The best regimen, in terms of specific drugs, drug/dose sequence, and route is not known at this time; also unknown is whether radiation therapy is necessary for all patients. However, neoadjuvant chemotherapy should be considered for patients who have traditionally been thought to be at high risk for local recurrence (i.e., patients with large, deep-seated, high-grade, extremity sarcomas). We believe that amputation should rarely be performed for large, high-grade, extremity soft-tissue sarcomas without first considering a trial of neoadjuvant therapy.

Unfortunately, we are still faced with limitations in the options for chemotherapy with only a small number of modestly active agents. For the future, more multicenter, prospectively randomized studies utilizing new, more effective chemotherapeutic agents, are needed.

OSTEOSARCOMA

Although osteosarcoma is a rare tumor, it is the most common malignant tumor of bone in adolescents and young adults. Approximately 1000 new cases occur each year in the United States.^{6,7} It is more prevalent in males and has a strong predilection for the distal femur, proximal tibia, and proximal humerus. About 80% of patients have localized disease at the time of diagnosis. The most common sites of metastasis are the lung and other bone.^{6,7,9,10}

Prior to 1970 the primary treatment of nonmetastatic osteosarcoma of the extremities consisted of surgical extirpation (usually amputation) and/or high-dose

radiation therapy of the primary tumor. The 5-year disease-free survival rate was no more than 20%; lung metastases were the most common reason for treatment failures. Early investigations of chemotherapy for osteosarcoma were unrewarding, and it was considered a chemoresistant tumor.^{75,76}

By the early 1970s, and continuing through the 1980s, reports began to emerge of effective drugs for the treatment of osteosarcoma, i.e., Adriamycin, high-dose methotrexate with calcium leucovorin rescue, cisplatin, and, more recently, ifosfamide.^{8,77-91} It was demonstrated that these agents could eradicate overt metastatic disease and improve disease-free survival,

Study design

- Preoperative chemotherapy – three cycles, q21 days
 - Cycle 1: Ifosfamide 2.25 g/m^2 IV qd over 2 h, days 1–4
 - Adriamycin 75 mg/m^2 CIV over 72 h
 - Cycles 2, 3: Adriamycin 75 mg/m^2 CIV over 72 h
 - Cisplatin 120 mg/m^2 IA over 4 h
- Surgery – Limb-sparing or amputation
- Postoperative chemotherapy – three cycles, q21 days
 - Cycles 4, 5, 6: Ifosfamide 2.25 g/m^2 IV qd over 2 h, days 1–4
 - Adriamycin 75 mg/m^2 CIV over 72 h

All cycles of chemotherapy are supplemented with G-CSF support at $5 \text{ } \mu\text{g/kg}$ SQ, starting 24 h after chemotherapy is finished.

Figure 3.1 WHC/WCI neoadjuvant chemotherapy for large, high-grade extremity soft-tissue sarcoma #2 (W94-3)

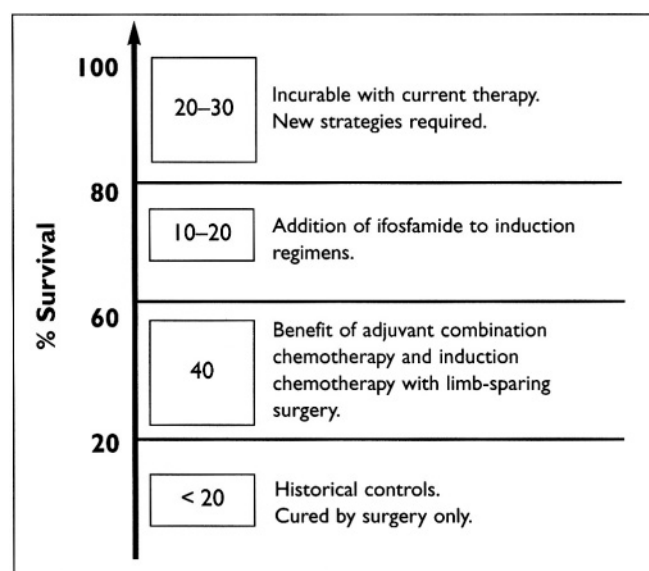


Figure 3.2 Development of treatment of patients with nonmetastatic osteosarcoma.

and they have been incorporated into modern chemotherapy protocols in varying combinations. To a large extent the major advances made over the past three decades in the treatment of osteosarcoma are a consequence of the development of effective chemotherapy. The introduction of these agents into multidisciplinary treatment strategies has allowed for more conservative and limb-sparing procedures to be performed and improved overall patient survival.⁶⁻¹⁰

Chemotherapy Development

There has been a wide variation in reported response rates to methotrexate (e.g. 0–80%), leading several investigators to question its effectiveness. The activity of methotrexate appears to be dose-dependent, given that dose escalation has been associated with responses in patients previously unresponsive to lower doses.⁷⁸ It has the significant advantage of being nonmyelosuppressive, but it is expensive and needs to be used with care and appropriate monitoring, especially in older patients. Rosen and others believe the variable response rates reported with methotrexate are directly related to improper drug administration.^{79,90} Several recent studies have shown that, in order for methotrexate to be effective in osteosarcoma, one must achieve a minimum peak serum concentration of greater than 1000 μmol (10^{-3} M) at the completion of a 4-h infusion (700 μmol after a 6-h infusion). To achieve these drug levels it is necessary to give a dose of at least 8–12 g/m². Furthermore, excessive amounts of IV hydration should not be administered during the first 24 h, in order to limit urine output to less than 1400 ml/m².⁷⁸⁻⁸⁵

Recently, Guo *et al.* have shown a high frequency (~65%) of decreased reduced folate carrier (RFC) expression in osteosarcoma biopsy samples, suggesting that the impaired transport of methotrexate is a common mechanism of intrinsic resistance in osteosarcoma.⁹² In addition, increased dihydrofolate reductase (DHFR) expression was found to be significantly higher in metastatic or recurrent tumor specimens but not in primary tumors.⁹² This may be a mechanism of acquired methotrexate resistance or reflect a possible difference between primary and metastatic tumors. These findings could help explain why higher doses of methotrexate with minimum peak serum levels (producing prolonged drug exposure) are required in order to obtain a good histologic response.

There also appears to be a steep dose–response rate for Adriamycin; i.e., doses ≥ 70 mg/m² have more activity than lower doses.⁷⁷ Whether carboplatinum can be substituted for cisplatin is still controversial. Carboplatinum has reduced renal and ototoxicity but produces more myelosuppression and may be less active than cisplatin.⁹³⁻⁹⁵ Initial reports indicated that the

combination of bleomycin, cyclophosphamide, and dactinomycin (BCD) was effective in the treatment of metastatic disease, and in several early preoperative studies this regimen was given with other known active agents. Subsequent studies failed to confirm the activity of BCD when given alone; consequently it is not included in most modern chemotherapy regimens.⁹⁶

Ifosfamide appears to have significant activity for the treatment of both primary and recurrent osteosarcoma. It also has a clear dose-dependent response curve (with responses occurring at doses of 12–18 g/m² in patients who had failed with previous doses below 10 g/m²).^{24-26,87-89} Further enhancements in patient outcome will most likely come from the inclusion of ifosfamide into newer combination regimens, and with the development of novel agents.

How best to combine these drugs is still unknown. There is still heated debate over what constitutes optimum chemotherapy. While most institutions utilize an intensive multi-agent regimen, some have questioned the merits of prolonged and complicated schemes over regimens that include fewer drugs given over a shorter time period.

A recently completed study by the European Osteosarcoma Intergroup (EOI) explored whether the intensive use of two active agents, cisplatin and Adriamycin, administered in six cycles over 18 weeks is better than a more complex, multi-agent modified Memorial Sloan Kettering Cancer Center (MSKCC) T10-like regimen given over 44 weeks.⁹⁷ There was poor patient compliance and a reduction in dose intensity with the multidrug regimen. The shorter, two-drug combination was found to have equivalent survival outcomes to that observed with the modified T10 program; the 5-year progression free and overall survival rates for both groups being only 44% and 55%, respectively. Unfortunately, these results are somewhat lower than that achieved in other previous studies. The EOI has since shown that the cisplatin/Adriamycin regimen can be safely intensified with G-CSF support.⁹⁸ Therefore, in its new study, the EOI will test the concept of dose density by randomizing patients to an induction cisplatin/Adriamycin regimen given every 3 weeks for two cycles or to the same regimen given every 2 weeks for three cycles with G-CSF support.

Adjuvant Chemotherapy

Once chemotherapy had been found to be effective against metastatic disease, investigations were initiated to determine the efficacy of these agents in destroying micrometastases, which are thought to be present in the majority of patients at the time of initial primary surgery (i.e., adjuvant or postoperative chemotherapy).⁹⁹ Five-year survival figures of 1286 patients

collected from the world literature between 1946 and 1971 showed a mean survival rate of 19.7% (range 16–23%).^{6,7} Eighty percent of patients developed metastases despite amputation, suggesting the presence of micrometastatic disease in the majority of cases.^{75,76}

In the 1970s, early uncontrolled adjuvant trials of single- and multi-agent chemotherapy regimens documented relapse-free survival rates of 35–60%.^{99,100} However, the contribution of adjuvant chemotherapy was then questioned by researchers from the Mayo Clinic, where the outcome with surgery alone was found to be improved (13% disease-free survival for patients treated in the 1960s compared with 42% for patients in the 1970s).^{101,102} Furthermore, a randomized adjuvant chemotherapy trial at the Mayo Clinic of moderate-dose methotrexate (considered inadequate by today's standards) versus surgery alone indicated no benefit for adjuvant chemotherapy. The relapse-free survival of the surgery-alone group was 44%, more than twice what was expected on the basis of the historical experience.

The exact role of adjuvant chemotherapy was then heatedly debated.^{101,103–106} Some felt that an increased survival for osteosarcoma patients had occurred over time. They believed that this was related solely to diagnostic advances in staging, the earlier detection of metastases, and to improvements in surgical techniques and supportive care.^{101,102} Prospective randomized controlled trials conducted by the Multi-Institutional Osteosarcoma Study Group (MIOS) and the UCLA group resolved this controversy when they confirmed the significant favorable impact of adjuvant chemotherapy on outcome.^{107–109} They also corroborated the poor prognosis for patients treated with surgery alone (Table 3.5).

Adjuvant chemotherapy has been shown to reduce the number of pulmonary metastases and to delay their appearance,^{110–115} thus possibly facilitating surgical removal. It has also changed the natural history of this neoplasm; more patients develop extrapulmonary metastases (e.g., to the skin, brain, and/or heart).^{112–115} The majority of trials of adjuvant chemotherapy now report event-free survival rates of 45–65%.^{99–100,103–109} Even with the increased use of preoperative chemotherapy to induce tumor necrosis, intensive adjuvant chemotherapy is still believed to be needed.

Induction Chemotherapy

At the same time that advances were evolving with chemotherapy, improved techniques of primary surgical resection were being developed that reduced the need for amputation. These new limb-sparing procedures required that surgery be delayed 2–3 months for the manufacture of a custom-made endoprosthesis. In the mid-1970s Rosen *et al.* at MSKCC designed a strategy to use induction (neoadjuvant) chemotherapy to treat patients who were awaiting manufacture of their prosthesis.¹¹⁶

The induction therapy approach had other potential benefits as well. It not only was felt to be an early defense against the possible presence of pulmonary metastases but also had the theoretical advantage of being able to reduce the emergence of drug-resistant tumor cells.^{116–120} It was also thought to help downstage a tumor by reducing the size of an accompanying soft-tissue mass and forming a surrounding reactive rim that would confine the tumor within a calcified periosteum. This could lead to better tumor demarcation and permit successful tumor removal with a

Table 3.5 Adjuvant chemotherapy for osteosarcoma – randomized studies

Study	Drug regimen	No. of patients	Percentage RFS	Percentage OS
Mayo Clinic ¹⁰²	HDMTX + VCR vs. no adjuvant therapy	38	40 <i>p</i> = NS 44 (6 years)	
MIOS ¹⁰⁸	BCD + HDMTX + ADRIA + CDDP vs. no adjuvant therapy	36 random 165 nonrandom	63 <i>p</i> = 0.001 12 (2 years)	71 <i>p</i> = 0.04 48
UCLA ¹⁰⁹	BCD + HDMTX + VCR + ADRIA (+ intra-arterial ADRIA + XRT) vs. no adjuvant therapy	59	55 <i>p</i> = 0.004 20	80 <i>p</i> = 0.04 48

RFS = relapse free survival, OS = overall survival, NS = not significant, HDMTX = high-dose methotrexate, VCR = vincristine, BCD = bleomycin, cytoxan, dactinomycin-D, ADRIA = Adriamycin, CDDP = cisplatinium, XRT = radiation therapy.

limb-sparing resection.^{12,119} In addition, it provided an opportunity to test chemotherapy sensitivity *in vivo* on the basis of the initial histologic response and then to customize or tailor adjuvant chemotherapy.¹²⁰

When intensive multi-agent regimens are used, induction chemotherapy trials have often produced better relapse-free survival rates (42–82%) than those reported for patients undergoing immediate surgery followed by adjuvant chemotherapy.^{12,118–132} Most modern induction protocols include a multidrug regimen, given for 6–18 weeks, followed by resection of the primary tumor and 3–8 months of adjuvant IV chemotherapy. Drugs used in these regimens include cisplatin and Adriamycin with or without high-dose methotrexate. Recent trials incorporating ifosfamide appear to have further increased tumor necrosis and improved patient survival.^{125,126,129,130} Nevertheless, patients need to be followed closely, since a small number may be completely insensitive to induction chemotherapy and the tumor may continue to progress. These patients need to be identified early so that they can be either switched to another chemotherapeutic regimen or have immediate surgical resection.

In conjunction with improvements in surgical technique and prosthetic devices, there has been a growing enthusiasm for limb-sparing surgery by orthopedic surgeons, which has also led to the more frequent use of induction chemotherapy. However, a number of key questions regarding induction chemotherapy remain, among which the most important are the following:

Histologic Assessment of Chemotherapy Response

The response of osteosarcoma to preoperative chemotherapy may be assessed by clinical, laboratory, radiologic, and pathologic parameters. Clinical responses are noted with a decrease in pain, swelling, and heat.¹³³ On laboratory analysis there can be a reduction of an elevated alkaline phosphatase.^{134,135} With plain radiography and computerized tomography scan, one can see a reduction or complete disappearance of any associated soft-tissue mass, revisualization of the fat planes between muscle bundles, healing of pathologic fractures, and organized deposition of calcium within the neoplastic bone (calcified periosteum) (Figures 3.3 and 3.4).^{136–139} An arteriogram can offer a less subjective means of assessing a tumor response; this can be manifest by a diminution or a disappearance of tumor vascularity and stain.^{137,140,141} Other techniques undergoing further evaluation include technetium-99 methylene diphosphonate functional imaging, gallium, thallium-201, and nuclear magnetic resonance scans.^{142–145}

Despite the utility of these various findings, the histologic appearance of the resected primary tumor specimen after induction chemotherapy has emerged as the gold standard for evaluating and measuring a therapeutic response. Several pathologic grading systems for assessing the effect of induction chemotherapy have been developed, all of which are based on the degree of tumor cellularity and necrosis found within the resected specimen.^{146–149} Grading systems can be imprecise, subjective, and prone to sampling errors. Nevertheless, with careful attention to adequate and precise sectioning from many sites of the surgical specimen, a determination of response can be assessed which appears to correlate with patient outcome.^{147–149}

The Huvo's grading system has served as a model for other systems.¹⁴⁶ A Grade III and IV response is characterized by an extensive or complete destruction of cells within the primary tumor and is associated with better survival (Figure 3.5). While a Grade I or II response is indicative of minimal destruction of tumor; these patients are more likely to develop distant metastases and have a poor survival. Unfortunately, the percentage of tumor necrosis is difficult to evaluate, and most investigators have not graded tumor necrosis in a similar fashion as first proposed by Huvo's and Rosen.¹⁴⁶ This ambiguity and variable definition of a good pathologic response (between 60% and 95% necrosis) amongst institutions and cooperative groups makes comparisons between different induction chemotherapy studies difficult.^{6,7,12}

Furthermore, of particular concern was an updated report from MSKCC suggesting a further modification of the Huvo's system. With larger patient accrual and longer follow-up, it was apparent that there was a greater difference in event-free survival in patients with a Grade III and IV response than between patients with a Grade II and III.^{121,150} Thus, it was felt that only patients with a Grade IV response should be considered as having a favorable prognosis, and if therapy were to be changed based on the degree of tumor necrosis following induction chemotherapy, it would be applied to all patients with less than Grade IV necrosis. For the future, an international standardized definition for a good pathologic response to induction chemotherapy is needed.

Tailoring Adjuvant Therapy

The concept of tailoring adjuvant therapy on the basis of the histologic response of the primary tumor to induction chemotherapy was first proposed by Rosen *et al.* and tested in the MSKCC T10 protocol.¹²⁰ This was formulated on the hypothesis that the responsiveness of the primary tumor to chemotherapy will predict that



Figure 3.3 Pathological fracture through a sclerosing osteosarcoma of the proximal humerus treated by induction chemotherapy. (A) Initial radiograph of the proximal humerus showing a sclerotic lesion within the medullary canal with a slightly displaced pathological fracture at the base (solid arrow). (B) Radiograph showing complete healing of the pathological fracture following three cycles of induction chemotherapy (consisting of Adriamycin, cisplatin, and ifosfamide). (C) Prechemotherapy angiogram showing marked vascularity of the tumor corresponding to the plain radiographs seen in (A). The axillary artery (curved arrow) gives rise to the circumflex vessels (small arrows) that feed the main tumor blush (large arrow). Most tumors of the proximal humerus have this vascular pattern. (D) Post-induction chemotherapy angiogram corresponding to Figure 3.3B showing complete avascularity of the tumor. This patient underwent a successful limb-sparing procedure with a modular proximal humeral replacement. There was 98–100% tumor necrosis (Huvos grade III to IV response). This patient remains free of disease at 24 months.

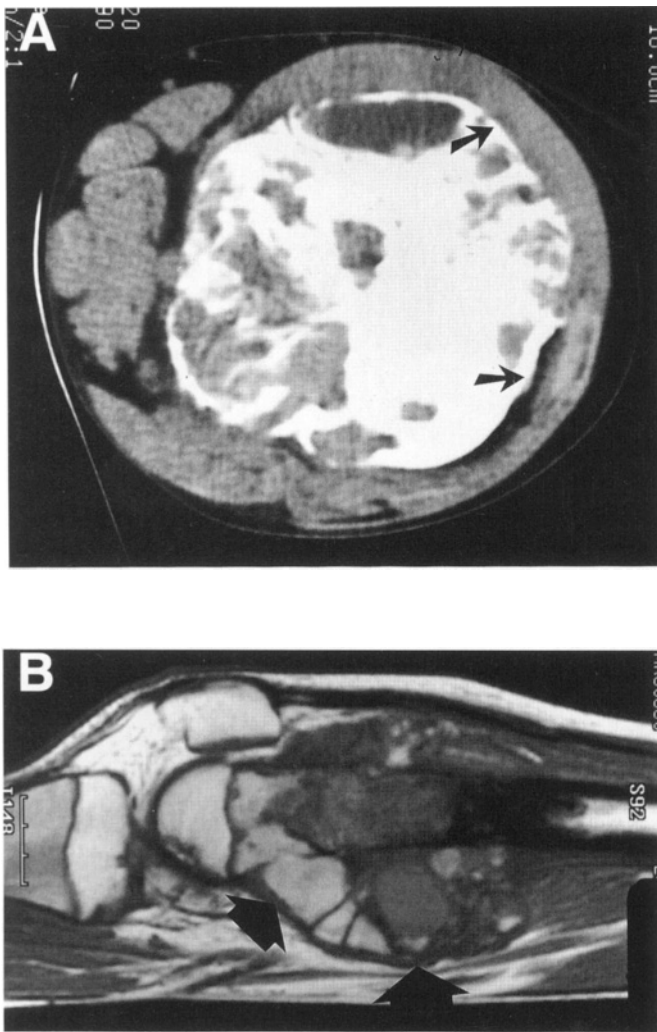


Figure 3.4 Typical radiographic response following induction chemotherapy. (A) CT scan of an extremely large tumor of the distal femur following induction chemotherapy. Note the complete sclerosis and rimming of the lesion (small arrows). A smooth rimming border is characteristic of a very high rate of tumor necrosis and an excellent chemotherapy effect. This patient underwent limb-sparing surgery with a distal femoral replacement in lieu of an initially planned high above-knee amputation. The amputation was initially considered due to the large size of the tumor. A vascular graft was not required. (B) MRI of the same patient shows a very typical black rimming response around the periphery of the tumor (solid arrows). MRI is not as reliable as CT in determining the response to chemotherapy. Although a solid black line around the periphery corresponds with the smooth cortical rimming seen on CT, this indicates the attempt of reossification and healing of the "tumor" defect.

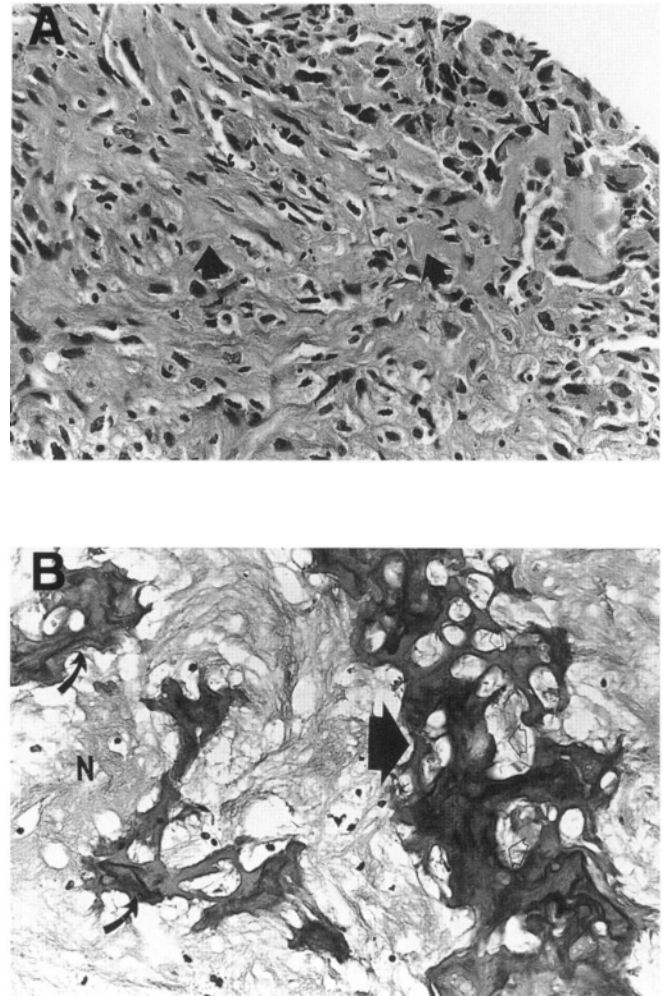


Figure 3.5 Histological effect of induction chemotherapy. (A) Osteosarcoma of the distal femur prior to chemotherapy. This photomicrograph shows completely viable tumor with early osteoid (solid arrows) formation. Note the pleomorphism and hyperchromatism. (B) Post-induction chemotherapy. This was obtained following a limb-sparing resection of the tumor. This section is representative of the entire tumor. Note that the stroma is completely necrotic (N) with several small, pignotic, dead nuclei seen. The remaining osteoid cells (large curved arrows) are present. There are no viable cells within the lacunae of the osteoid matrix. This is a very typical appearance of a good killing effect by the chemotherapeutic agents. The stroma cells die and are replaced by a fibrovascular stroma but the osteoid matrix remains. Clinically, an osteosarcoma with a good response to chemotherapy may shrink no more than 20–25%. This is explained by the fact that the remaining osteoid does not resolve (hematoxylin and eosin stain; original magnification $\times 100$).

of micrometastases. Thus, a good-responding patient receives the same drugs after surgery as before surgery, while the postoperative regimen of a patient who has responded poorly to induction chemotherapy is changed. Early results by Rosen *et al.* from the T10 protocol reported an excellent disease-free survival rate for poor-responding patients as well, suggesting that they could be salvaged with a modified adjuvant (postoperative) treatment.¹²⁰

The T10 protocol was a model for many trials launched in the 1980s, virtually all of which featured induction chemotherapy and the individualization of postoperative therapy on the basis of the pathologic responsiveness of the primary tumor.^{117–120} Unfortunately, later studies from several groups, including the Children's Cancer Study Group (CCSG), German–Austrian–Swiss Cooperative Osteosarcoma Study Group (COSS-82), and the Rizzoli Institute, failed to confirm an improved prognosis for poor responders treated with alternative postoperative chemotherapy regimens.^{118,119,123,127} Furthermore, an update of the MSKCC T10 protocol, reported by Meyers *et al.*, indicated that Rosen's promising preliminary results were not sustained over time. With longer follow-up the efficacy of tailored treatment was not demonstrated.¹²¹

However, a recent study by Benjamin *et al.* from MDACC suggests that the addition of postoperative ifosfamide significantly improved the 5-year disease-free survival of poor-responding patients over that seen in their previous treatment regimens (67% vs. 34%, respectively, $p = 0.015$).¹²⁶ Other recent studies incorporating ifosfamide have documented better survival rates, and it appears that there may be further benefits if this agent is added to induction therapy as well.^{125,128–130,132}

Duration of Induction Chemotherapy

There is considerable variability in the duration of induction chemotherapy. Most studies use an arbitrary time of 6–18 weeks with the administration of two to six cycles of chemotherapy. Some investigators have attempted to adjust surgical intervention to the time of maximal response to induction chemotherapy. Longer-duration chemotherapy regimens may be associated with a higher proportion of good histologic responses; however, as the duration of induction chemotherapy is prolonged, the value of using its effect on histologic response as a predictor of patient outcome may be lost. Thus, regimens of longer duration may result in a better histologic response, but this may not translate into improved patient survival. Meyers *et al.* have suggested that the rate of a good histologic response may be related to the duration of induction chemo-

therapy, but that the duration of chemotherapy does not correlate with relapse-free survival.¹³¹

Induction/Adjuvant Chemotherapy versus Adjuvant Chemotherapy

Some investigators have felt that the superior results obtained with induction chemotherapy may simply reflect the use of more intensive multi-agent chemotherapy (i.e., cisplatin and ifosfamide) and may be unrelated to the timing (preoperative versus postoperative) or route of administration of chemotherapy (IV versus IA).^{7,151} They have argued that equally intensive adjuvant chemotherapy regimens need to be tested against induction chemotherapy in a prospectively randomized fashion. Retrospectively, it appears that patients treated with induction chemotherapy have fared better than patients treated with immediate surgery and postoperative adjuvant chemotherapy. However, the majority of induction chemotherapy trials have been single-institutional studies, which inherently are known to yield better results because of patient selection. By contrast, the majority of adjuvant chemotherapy trials have been multi-institutional or cooperative group studies (Table 3.6).

The Pediatric Oncology Group (POG) performed a randomized trial of induction versus adjuvant chemotherapy.¹⁵¹ Patients were randomized to immediate surgery or to presurgical treatment with two cycles (10 weeks duration) of high-dose methotrexate, cisplatin, and Adriamycin. Except for timing, postsurgical chemotherapy (methotrexate, cisplatin, Adriamycin, and BCD), given over 44 weeks, was the same in both arms.

The survival rate for the group receiving induction chemotherapy was no better than that of the adjuvant chemotherapy alone group (Table 3.7). Whether induction chemotherapy improved the limb salvage rate has not yet been reported. Poor responders in the induction arm were not crossed over to other agents; thus, the strategy of salvage therapy was also not evaluated.

Table 3.6 Chemotherapy trials for non-metastatic osteosarcoma (with >50 patients)

	Composite 5-year disease free survival
Adjuvant (mostly multi-institutional, cooperative groups)	46–61 %
Neoadjuvant + adjuvant (mostly single institutions)	49–80 %
POG #8651 – randomized trial	Same – no difference

Table 3.7 POG #8651 – 100 evaluable patients

Chemotherapy regimen	% 5-year survival	
	Disease free	Overall
Induction and adjuvant	63.2	79.7
Adjuvant	65.5	75.3

Goorin A *et al.*, Med Ped Oncol. 1996;27:263a.

Some have cited this study as a reason not to give induction chemotherapy since there was no improvement in patient survival. On the other hand, the results suggest that induction chemotherapy may have improved the limb-salvage rate and extremity function without compromising overall survival, as was initially feared.

Intra-arterial Chemotherapy

To improve the results of induction IV systemic chemotherapy, to further downstage tumors, and to augment the rate of successful limb-sparing procedures, several investigators began to administer induction chemotherapy via the IA route.¹² This allows for a higher concentration of chemotherapy to be delivered to the primary tumor, with possible improved penetration of drug across the cell membrane.^{152–154} Pharmacologic studies have confirmed an increased regional drug concentration, drug uptake, and tumor destruction when the IA route is utilized.^{133,152–154} Furthermore, the concentration of chemotherapy reaching the systemic circulation after initial intra-arterial passage has been found to be similar to that attained via the IV route and therefore should be enough to destroy any microscopic pulmonary metastases.^{133,152–154}

Initial IA studies utilized Adriamycin, but this treatment was complicated by erythema and ulceration of the underlying skin and subcutaneous tissue, with extensive necrosis of normal tissue. A complete histologic response in the primary tumor was rarely obtained.^{155–157} Because of the potential for normal tissue destruction, preoperative IA Adriamycin was not endorsed or accepted.¹²

Cisplatin is an alternative drug for IA use. Jaffe *et al.* established the use of IA cisplatin as a single agent for the treatment of osteosarcoma in the pediatric population.^{153,158} When this drug was given alone, at least four courses were required to achieve an optimum effect. In a study comparing cisplatin and high-dose methotrexate, a greater proportion of patients were

found to respond to IA cisplatin, with a significantly higher number of pathologic good responders ($\geq 90\%$ tumor necrosis).¹⁵⁹ Unfortunately, there was still a high rate of metastases (almost 50%).

Others have given IA cisplatin concurrently with different IV systemic agents.^{12,160–169} Small single-institution studies suggest that this allows for more limb-sparing procedures to be performed and does not substantially increase the risk of local recurrence or the development of metastatic disease. Such an approach has been associated with a higher tumor necrosis rate, perhaps making it possible to convert a marginal resection to a wide resection and to allow for a safer surgical procedure to be performed.¹⁶⁹ Relapse or disease-free survival (DFS) rates for single-institution IA studies appear to be similar to those using IV induction chemotherapy (with DFS rates in the 43–89% range).¹²

To date, the use of IA chemotherapy has been limited to centers with excellent angiographic support and facilities. There is a need to determine whether the cost, complexity, time commitment, and morbidity associated with this approach are justifiable. A prospective randomized study from the Rizzoli Institute reported that patients who received induction IA cisplatin had a significantly higher proportion of good histologic responses than those who received similar doses of IV cisplatin.¹²⁴ There did not appear to be any differences between the two groups in the number of limb-sparing operations, and the follow-up period was too short to determine a difference in survival (Table 3.8).

In a second study (COSS-86) investigating the use of more intensive preoperative chemotherapy, Winkler *et al.* compared the effects of cisplatin given by IA tourniquet infusion or by IV infusion (Table 3.8).¹³² Following cycles of IV Adriamycin and methotrexate, cisplatin was administered over 1 h with concomitant IV low-dose ifosfamide (6 g/m^2). These authors confirmed the results of previous researchers by showing that the amount of drug available to act against micrometastatic disease was not compromised by regional therapy. They found an identical systemic availability for cisplatin; plasma, ultrafiltrate, and urinary concentrations were similar, regardless of the route used. There was also no correlation between the deposition of cisplatin in tumor tissue and the mode of cisplatin administration or the histologic response. When pharmacokinetic data showed equal systemic drug availability for both routes, the dose was reduced from 150 to 120 mg/m^2 . Additionally, the IV cisplatin infusion was extended from 1 to 5 h in order to decrease ototoxicity.

The original efforts to randomize patients onto this study were not successful, and randomization was abandoned in favor of central allocation (with an

Table 3.8 IV vs. IA cisplatinum neoadjuvant chemotherapy for osteosarcoma

	IV	IA	p-Value
Rizzoli Inst. Regimen – HD–MTX, ADR, CDP 120 mg/m ² /CI 72 h IV or IA			
Histologic good response (no. of patients)	46% (18/39)	78% (31/40)	0.004
COSS-86 Regimen – HDMTX, ADR, IFOS, CDP 120–150 mg/m ² IV or IA			
Limb-salvage surgery	28% (20/72)	54% (30/56)	0.007
Local recurrence	4% (3/68)	0% (0/56)	NS
10-year DFS	70%	63%	0.453 NS
10-year OS	75%	67%	0.335 NS

Bacci G *et al.* J Chemother. 1992;4:189–95.

Fuchs N *et al.* Ann Oncol. 1998;9:893–9.

NS = not significant; DFS = disease free survival; OS = overall survival; HDMTX = high dose methotrexate; ADR = adriamycin; IFOS = ifosfamide; CDP = cisplatinum

attempt to balance for patient age and sex, tumor site and size). Furthermore, all high-risk patients who received only one IA treatment were included in the comparison. Limb-salvage surgery was possible more often after IA than after IV treatment (Table 3.8). There were fewer local recurrences in the IA group, but the difference did not reach statistical significance. There was no significant correlation between the route of administration and survival, although outcomes were slightly poorer for patients treated intra-arterially. This study has been cited as a fully prospective, randomized trial, but when the original plan for randomization was discarded, a selection bias could have been introduced despite the efforts of each study center to try to obtain balanced groups.

Any further benefits of IA induction chemotherapy will require prospective randomized investigation. Thus far, it has not appeared to make a significant difference in terms of disease-free and overall survival. It is also possible that future studies with more intensive multi-agent IV chemotherapy (i.e., high-dose ifosfamide) could negate any IA effect.

Incorporation of Ifosfamide into Induction Multi-agent Regimens

For many years the main strategy used to improve survival in osteosarcoma patients was to modify the postoperative chemotherapy regimen of those with a poor histologic response to induction chemotherapy. As mentioned previously, except for more recent regimens that contain ifosfamide, the effect of conventional salvage treatment is questionable.

An obvious alternative to salvage chemotherapy is to use new active agents up-front during induction chemotherapy. Miser *et al.* achieved excellent long-term

results by incorporating ifosfamide concomitantly with Adriamycin into a 14-week induction regimen that included high-dose methotrexate.¹²⁹ Cisplatinum was added postoperatively only for poor histologic responders. Seventy-six percent of patients had $\geq 95\%$ tumor necrosis; relapse-free and overall survival rates at 6 years were 73% and 88%, respectively. Bacci *et al.* have shown independently that adding ifosfamide to an induction chemotherapy regimen significantly improved the limb-salvage, histologic response, and disease-free survival rates when compared with their previous study in which ifosfamide was given only after surgery (Table 3.9).¹³⁰

Patel *et al.* are attempting to improve the survival of osteosarcoma patients known to have a poor prognosis (e.g. patients with the large pelvic/axial primary tumors or with metastases at presentation) using an intensive multi-agent induction regimen that includes cisplatinum, Adriamycin and high-dose ifosfamide with peripheral blood stem cell and G-CSF support.¹⁷⁰

In summary, the prognosis for patients with osteosarcoma of the extremities has markedly improved over the past three decades. More than two-thirds of patients who present with nonmetastatic disease are now cured (Figure 3.2). These advances are mainly due to the use of intensive multi-agent chemotherapy. The impact of adjuvant chemotherapy is now indisputable, and it has become part of standard treatment. It is not yet clear which combination or duration schedule of chemotherapy is the best (among cisplatinum, Adriamycin, and high-dose methotrexate), but it does appear that the addition of ifosfamide further improves overall patient survival.

Limb-salvage surgery is now an accepted practice by orthopedic oncologists for the majority of osteosarcoma patients. Many centers also administer induction

Table 3.9 Addition of ifosfamide to neoadjuvant chemotherapy for osteosarcoma

	OS-3: HDMTX, CDP, ADR + post-op IFOS	OS-4: HDMTX, CDP, ADR, pre and post-op IFOS	p-Value
Limb salvage	83%	95%	0.004
Total necrosis	17%	32%	0.005
Good response	55%	83%	
Local recurrence	5%	6%	NS
2-year disease-free survival	68%	85%	0.003

Bacci G *et al.* Acta Oncol. 1998;37:41–8. NS = not significant

chemotherapy in order to enhance limb-salvage opportunities, although its role in further improving patient survival remains uncertain. The question of a possible advantage of IA over IV cisplatin remains unresolved because of a lack of properly randomized prospective studies. However, any positive effect of the IA route may be nullified by the inclusion of ifosfamide into new IV induction regimens. The benefit of tailoring adjuvant chemotherapy on the basis of the histologic response of the primary tumor to induction chemotherapy has not been fully substantiated. New markers are needed that can conclusively predict the histologic response and prognosis of patients at diagnosis, prior to induction chemotherapy, such that patients can be stratified into high- and low-risk subgroups.^{171–177}

Finally, despite the enormous progress that has been made, we are still faced with limitations in the options for chemotherapy because of the small number of modestly active chemotherapeutic agents. There is a need for new drugs and strategies to treat those patients already known to have a poor prognosis (e.g., large pelvic/axial tumors, metastases at presentation) earlier in the course of their treatment.^{178–180}

New Developments and Approaches for Sarcoma Treatment

In the future, therapy for sarcomas should be enhanced by advances in pharmacology, cell biology, immunology, and molecular genetics that will lead to more efficacious, specific, and less toxic treatments (Table 3.10).

Higher doses of ifosfamide have already been incorporated into many front-line regimens.^{47–50,170} The resultant cumulative thrombocytopenia could be ameliorated with more specific growth factors (i.e., thrombopoietin) and/or stem cell infusion. New platinum analogs may prove to have equal or more activity than cisplatin, and be less toxic. With the identification of one of the mechanisms of primary drug resistance being mediated through p-glycoprotein, new

Table 3.10 New developments and strategies for sarcoma therapy

- (1) *Chemotherapy*
 - (a) Dose intensification with hematopoietic growth factor and/or PBSC support
 - (b) Reversing multidrug resistance
MDR Inhibitor (e.g., PSC-833, Incel)
- (2) *Angiogenesis inhibitors*
- (3) *Growth factor manipulation*
 - Liposarcoma – ligand activation of PPAR
 - Troglitazone – stimulates adipose differentiation
 - Osteogenic sarcoma – Somatoline → decrease IGF-I
 - Herceptin
- (4) *Immune modulation*
 - L-MTP-PE
 - Immunotoxins
 - Nonmyeloblastic allogeneic transplant
- (5) *Utilizing oncogene products*
 - Modifying tumor suppressor genes
 - Antisense oligonucleotides
 - Vaccines to tumor-specific fusion peptides

strategies have evolved to reverse the multi-drug resistant phenotype with inhibitor agents (e.g., cyclosporin, PSC-833, Incel).¹⁸¹

Cell biology studies have further elucidated several growth factors and receptors that play critical roles in sarcoma cell proliferation and differentiation. In preadipocytes it has been shown that stimulation of the peroxisome proliferator activated receptor-gamma (PPAR- γ) induces terminal differentiation. Troglitazone, an oral antidiabetic agent and a PPAR- γ ligand, is being evaluated in order to promote differentiation in patients with incurable liposarcomas.^{182,183}

Insulin-like growth factor (IGF-1) has been found to be a potent mitogen for osteosarcoma cells *in vitro*, and growth hormone (GH) is a major regulator of IGF-1.¹⁸⁴ In a murine osteosarcoma model, modulation of the GH/IGF-1 axis by hypophysectomy reduced local growth and inhibited metastases.¹⁸⁵ The Pediatric NCI Group is utilizing a somatostatin analog to block GH release (indirectly reducing IGF-1 production) in order to prevent the development of lung metastases in osteosarcoma patients who have received adjuvant chemotherapy.¹⁸⁶

Recently, the over-expression of the Her-2-neu (human epidermal growth factor 2) receptor has been identified in tissue samples from approximately 40% of osteosarcoma patients. It was found to be associated with a poorer histologic response to chemotherapy and decreased event-free survival.^{176,177} In breast cancer the results of clinical trials of an antibody that targets this receptor, herceptin (rhMAB HER2, recombinant humanized anti-HER2 monoclonal antibody), used as a single agent or in combination with chemotherapy, have been encouraging. Furthermore, there appears to be synergy when herceptin is used with cisplatin.¹⁸⁷ These findings have led to new Phase II single-agent trials for patients with refractory or recurrent osteosarcoma and, in combination with chemotherapy, for newly diagnosed patients who have poor prognostic factors.

Since several types of sarcomas are known to be quite vascular and the majority of recurrences are systemic, the role of angiogenesis inhibitors in controlling sarcoma growth is of great interest. Interferon alpha has been shown to have weak antiangiogenic effects and only minimal activity.^{48,188} However, new compounds, including the matrix metalloproteinase inhibitors, vitaxin (monoclonal antibody to endothelial cell integrin), anti-VEGF (vascular endothelial growth factor), endostatin, and thalidomide, are being evaluated not only to prolong disease stabilization but also to reduce tumor growth.⁴⁸ The ultimate goal is to use these agents in the adjuvant setting.

Translational research in immunotherapeutic technology has also advanced. Kleinerman *et al.* have shown that the biologic response modifier L-MTP-PE (liposome-encapsulated muramyl tripeptide phosphatidylalanine), a component of *Mycobacterium*, can activate pulmonary macrophages to a tumoricidal state and prevent or reduce the incidence of lung metastases in both canine and human studies.^{189,190} A current Intergroup (CCSG and POG) trial is evaluating whether the addition of this biologic response modifier,

given after adjuvant chemotherapy, will improve relapse-free survival.

Most human sarcoma cells express class I and/or II MHC and HLA class I and II antigens that can be recognized by cytotoxic CD8+ and CD4+ T cells.¹⁹¹ On the basis of initial promising results in renal cell cancer by the National Heart, Lung and Blood Institute (NHLBI) Transplant Group, our institution and the NHLBI will be investigating the use of nonmyeloblastic allogeneic transplantation followed by donor lymphocyte infusion in order to elicit an anti-tumor immune response through a donor graft versus sarcoma effect.^{192,193}

Cytogenetic analyses of sarcomas have identified distinct chromosomal translocations that appear to encode for tumor-specific fusion proteins associated with certain histologic subtypes (e.g., synovial sarcoma – t(X;18), SYT/SSX1; Ewing's sarcoma – t(11;22), EWS/FLI-1).¹⁹⁴ These characteristic and consistent genetic changes not only transform cells to the malignant phenotype but also could result in tumor-specific antigens that are potential targets for immune-based therapy (e.g., immunotoxins, vaccines, and antisense oligonucleotides against the fusion RNA).^{191,194} In addition, tumor suppressor genes (i.e., p53, Rb1) have been found to play critical roles in sarcoma growth inhibition. Reintroduction of wild-type genes such as p53 *in vivo* could lead to complete tumor regression or sensitization of resistant tumors to existing chemotherapy.¹⁹⁴

CONCLUSIONS

The prospects for further understanding the clinical and molecular behavior of this complex group of rare tumors appear promising. Most likely, therapy will become more individualized based on the biology and chemosensitivity of different sarcoma subtypes. Such a development would be analogous to what has occurred in the treatment of non-Hodgkin's lymphomas. It is hoped that the dramatic surgical advances that have been made in limb salvage will be surpassed by significant discoveries in the control of systemic disease.

As we enter a new millennium, the treatment of patients with sarcomas will require collaboration among a variety of different health professionals and researchers. An interdisciplinary team approach will be necessary in order to advance the goals of local tumor control, limb salvage with optimum extremity function, minimal morbidity from treatment, and improved long-term survival.

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4

Isolated Limb Perfusion in the Treatment of Advanced Soft-tissue Sarcomas

Joseph M. Klausner, Dina Lev-Chelouche, Isaac Meller, Moshe Inbar and Mordechai Gutman

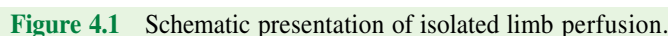
BACKGROUND

In 1958, Creech and Krementz¹ introduced a novel method of drug delivery for patients with advanced cancer and named it isolated limb perfusion (ILP).¹ The idea was to apply the newly invented technique of cardiopulmonary bypass to regional chemotherapy. ILP entailed exposing the major blood vessels to an extremity, isolating it temporarily and perfusing the extremity via a heart–lung machine with very high doses of chemotherapeutic drugs (Figure 4.1). The authors believed it would be possible to obtain high tissue concentrations of the drug with minimal systemic exposure and hence few complications. Following the observation that heat has its own antineoplastic properties, Stehlin² in 1969 modified the technique to include hyperthermia.

The response rates observed with ILP in patients with metastatic melanoma confined to the limb were higher than those associated with any other known modality. This, combined with the fact that some 25% of complete responders have a 10-year disease-free interval, promoted the use of ILP. Since then, ILP has been widely recognized as a standard treatment strategy for advanced melanoma of the extremities.

Despite its effectiveness, ILP did not become widely used, and several major cancer centers did not include it in their therapeutic arsenal. There are several reasons for this. ILP is a multidisciplinary procedure. It is surgically demanding and rather long (3–4 h). It necessitates a heart–lung machine and related technician and equipment, and isotopic monitoring. Unlike the reasonable ease with which new operative techniques are implemented through the acquisition of knowledge and skills, ILP requires a thorough knowledge of vascular surgery and a large degree of coordination and dependence on other disciplines outside the realm of general surgery. In addition, the available literature on ILP showed great variability in surgical technique, drugs administered, degree of hyperthermia, indications, and response evaluation. This, coupled with the retrospective nature of most reported patient series, made it difficult to reach valid conclusions as to when and how to use ILP.

The situation has gradually changed, mainly because of two advances. First, the standardization of ILP and the conduct of multicenter studies based on principles of modern surgical oncology and consistent with the standards of the National Cancer Institute made it possible to evaluate outcomes in a uniform fashion, and hence to better define the indications for ILP. The second advance was the addition of tumor necrosis factor (TNF), an exciting new cytokine, to the treatment protocols.³ TNF is a new drug and its potentially serious side-effects necessitated modifications to the ILP technique. Therefore, all centers began to routinely monitor ILP patients for isotope leakage and better standardization was achieved.



Preparation

Ulcerated or infected tumors should be recognized as a septic risk. The existing bacterial colonization may turn into overt sepsis or abscess formation following the induction of rapid necrosis with TNF or chemotherapy. Cultures and preoperative antibiotics are routinely required.

Patient evaluation and preparation are similar to those preceding any major surgical procedure. Specific attention must be given to the peripheral vascular system. Evidence of peripheral vascular disease may require further evaluation by angiography. Patients with severe arteriosclerotic disease, especially those with

Evaluation of the venous system for deep thrombosis (DVT) by ultrasound Doppler is important, particularly in patients who have undergone prior surgery or ILP to the affected limb. Since the adequacy of perfusion depends on the patency of the venous system, patients with DVT are poor candidates for ILP. Finally, the neurological status of the limb should be carefully recorded, particularly in patients with prior surgery, radiotherapy, or tumors adjacent to the nerves. Limb volume should be measured or calculated, because the drug dosage used during ILP is based on the volume of the extremity.⁴ Limb volume can be measured using the water displacement method, in which the extremity is immersed in a calibrated cylinder filled with water. Alternatively, it can be calculated by measuring limb length and circumference at multiple points and incorporating them into a mathematical formula used for calculating the volume of a cylinder.

The patient should be fully informed of the procedure. Such explanations should emphasize short-term and particularly long-term complications, that may be associated with the procedure.

Table 4.1 Site distribution of 228 limb perfusions*

Perfusion site	Melanoma	Sarcoma
Lower limb	89	88
Iliac	61	47
Femoral	18	22
Popliteal	10	19
Upper limb	33	18
Subclavian	24	11
Brachial	9	7

* Author series 1990–98.

Selection of the Procedure

ILP can be performed through various sites (Table 4.1). For the lower limb it is done via the external iliac, common femoral or popliteal vessels; for the upper limb it is performed via the brachial, axillary or subclavian vessels. The level of perfusion should be based on the nature and extent of the tumor, as well as technical considerations such as prior surgery or radiotherapy.

Because the majority of ILP candidates are patients with melanoma of the lower limb, the most common route of perfusion is the external iliac vessels. For patients with soft-tissue sarcomas (STS), more distal sites for cannulation may be chosen that are proximal to the tumor mass. Perfusions via the popliteal or brachial vessels are considered simpler, despite the smaller diameter of the vessels, because these vessels are usually accessible with less dissection and accommodate the use of a tourniquet applied proximally on the thigh or arm to ascertain complete isolation and avoidance of systemic leakage.

Surgery

ILP entails major surgery and is performed under endotracheal general anesthesia. Given the need for systemic heparinization, epidural and regional anesthesia are not recommended.

In the operating room the entire extremity is scrubbed. Four thermistor probes are inserted; two into the subcutaneous tissue and two into the muscles, in the distal and proximal parts of the extremity, respectively, to measure limb temperature during the procedure. A heating blanket is wrapped around the limb and sterile draping is applied on top of it. It is important that the limb can be manipulated and positioned during the procedure to permit the application and wrapping of the Esmark band on its root. For distal (popliteal/brachial) cannulations, a pneumatic tourniquet is applied proximal to the operative site (Figures 4.2A, 4.2B).

Lower Limb Perfusion

Iliac Perfusion

An oblique incision is made in the iliac region. The fascia and muscles are sectioned and the retroperitoneum is entered. The peritoneum is retracted medially. After exposing the external iliac vessels from their origin to the inguinal ligament, the vessels are dissected circumferentially and all side branches, including collaterals situated behind the inguinal ligament (i.e. the epigastric, obturators, deep internal and external circumflex vessels), are ligated and sectioned. All branches, especially from the posterior aspect of the external iliac vein, should be ligated. These deep collaterals are not affected by external Esmark banding, and their control is crucial for minimizing leakage during perfusion. Ligation of the internal iliac vein is optional (Figure 4.2C).

Upper Limb Perfusion

Axilla

The vessels are dissected circumferentially, and all collaterals are ligated and divided. The artery and vein are then clamped proximally and cannulated (8–14F). The tips of the cannulae are directed towards the proximal portion of the arm. An Esmark tourniquet is wrapped tightly around the root of the shoulder and anchored with Steinmann pins inserted into the skin below and lateral to the breast. Because the shoulder is smaller than the root of the lower limb, isolation and control can be achieved more easily in the arm than in the leg.

Brachial Perfusion

This is performed through a longitudinal incision in the medial aspect of the arm. Smaller cannulae adjusted to the vessel size are chosen. Minimal dissection and collateral ligation are required since complete isolation is easily achieved with the aid of a small pneumatic (blood pressure) tourniquet applied proximally and inflated to 250–300 mmHg.

Extracorporeal Circulation

The extracorporeal system consists of a roller-pump similar to that used for cardiopulmonary bypass surgery (Figure 4.2D). A single-head pump is sufficient. The pediatric surgery disposable pack, with its smaller-sized oxygenator, venous reservoir and tubing, is most suitable. A heat exchanger is required to warm the perfusate to 42°C. Priming is with 700–1000 ml of balanced electrolyte solution, one unit of packed RBCs and 1500 U heparin. Dextran (Haemacel®) can be used

to replace blood. Mild hyperthermia (39–40°C) is used; true hyperthermia (41–42°C) is rarely used because it produces severe limb toxicity.

Limb temperature is increased by heating the perfusate to 42°C and by applying the heated blanket and draping it around the limb. The temperature probes enable close monitoring.

The first stage of ILP is devoted to heating the perfusate and assessing leakage. Significant time may be required to warm skin temperature to 39°C. Leakage from the limb is dependent on the perfusion flow rate.⁵ Experience with high perfusion flow rates (700–1300 ml/min and 300–600 ml/min for the lower and upper limbs, respectively), resulted in relatively high systemic leakage rates ($12.5 \pm 2.9\%$) and consequently severe systemic toxicity. Decreasing the perfusion flow rate to 400–500 ml/min and 150–300 ml/min for the lower and upper limbs respectively, reduced leakage and systemic toxic effects. Increased pressure may contribute to leakage by opening up vessels and forcing blood through small collaterals in subcutaneous tissues, muscles, and vessels along the periosteum between the limb and major vasculature.

This is likely with high flow rates that may induce venous pressure in the perfused limb that exceed that of the systemic pressure (Figure 4.2E).

Leakage Monitoring and Adjustment

The patient is continuously monitored to ensure that the perfusate does not leak into the circulatory system. Such monitoring was not routinely done prior to the TNF era, and surgeons relied simply on stable reservoir volume and their own personal experience to estimate leakage. With TNF, leakage monitoring became mandatory. Protocols using microlabeled albumin or technetium-labeled RBC are used for monitoring leakage during ILP.^{6,7} After establishing perfusion with a stable flow and venous reservoir volume, the isotope is injected into the perfusate. A gamma camera is positioned over the precordial area and the head. Any increase in counts over the background signifies a systemic leak. A leak of less than 1% can be detected, allowing rapid adjustments to limit side-effects. Another indication of leakage is alterations in the calibrated venous reservoir volume, which drains the

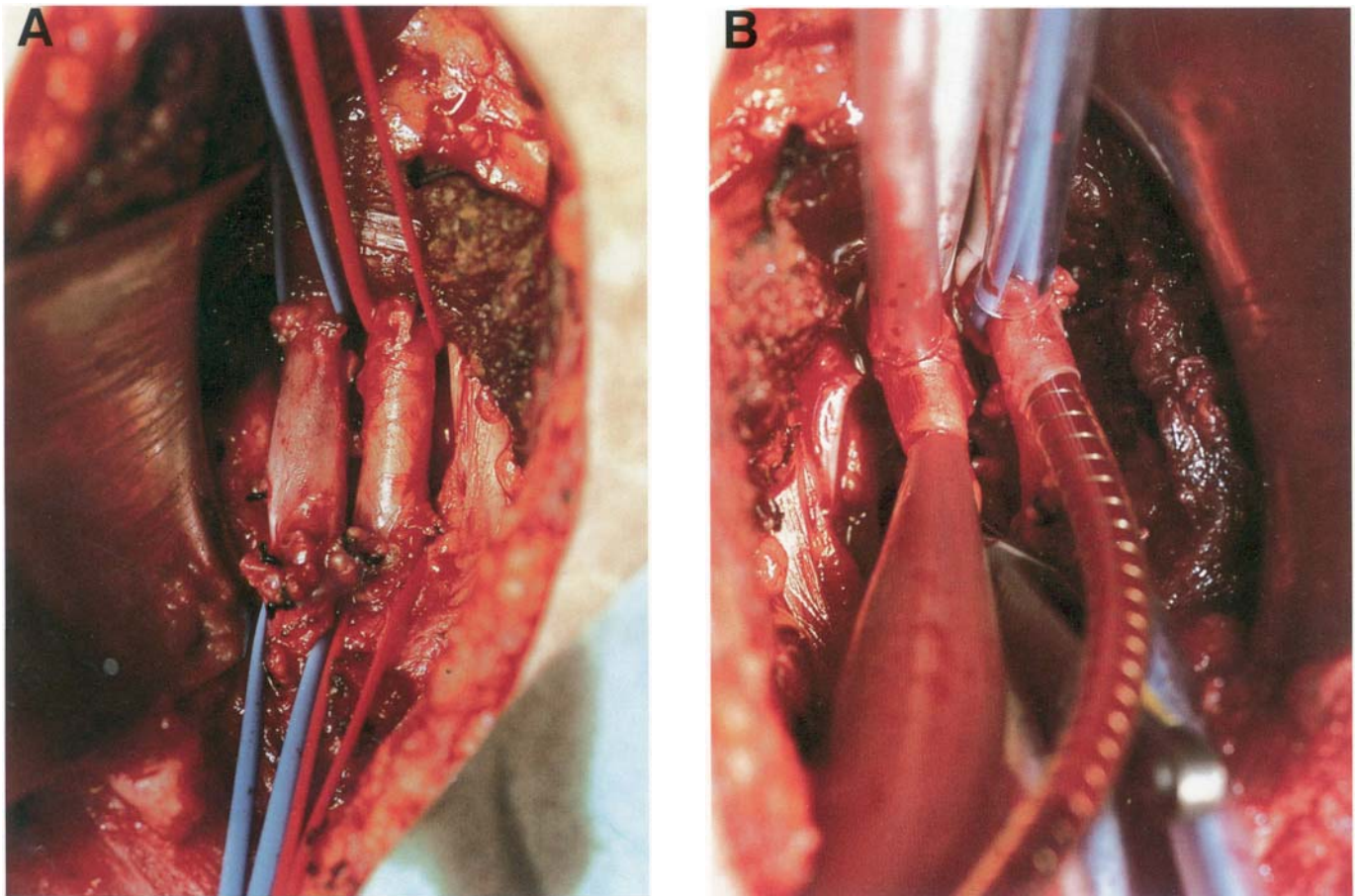
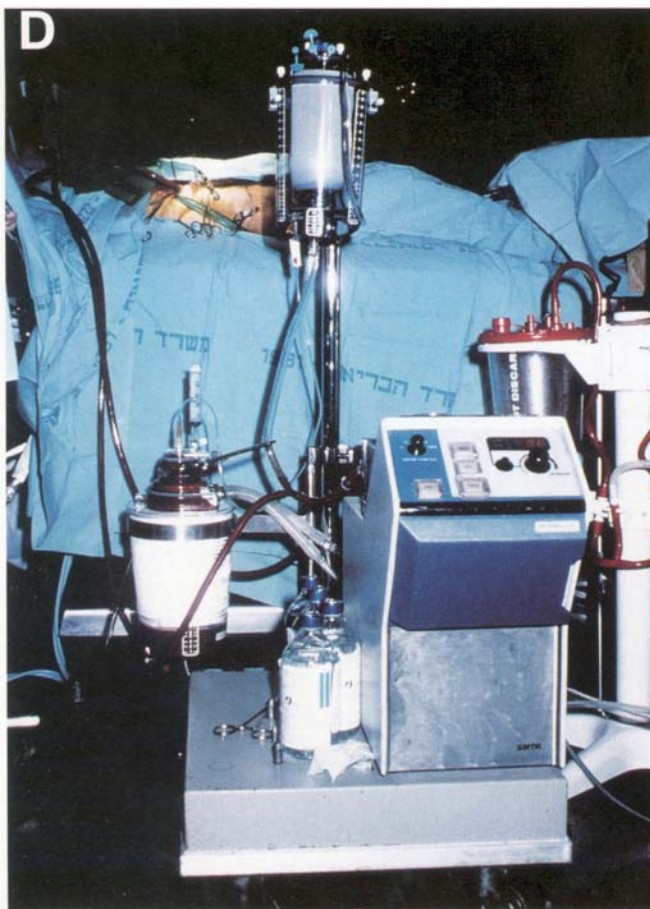
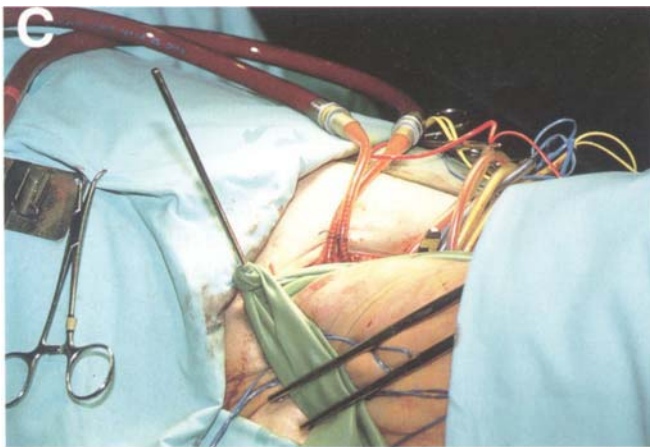


Figure 4.2 A,B (see above and following page)



venous effluent by gravity. A decrease in reservoir volume indicates a leak from the perfused limb into the systemic circulation, whereas an increase in venous reservoir volume signifies a leak from the systemic circulation into the limb.

With the information provided from monitoring, and the volume of the venous reservoir, it is possible to manipulate the perfusion rate and minimize leakage.

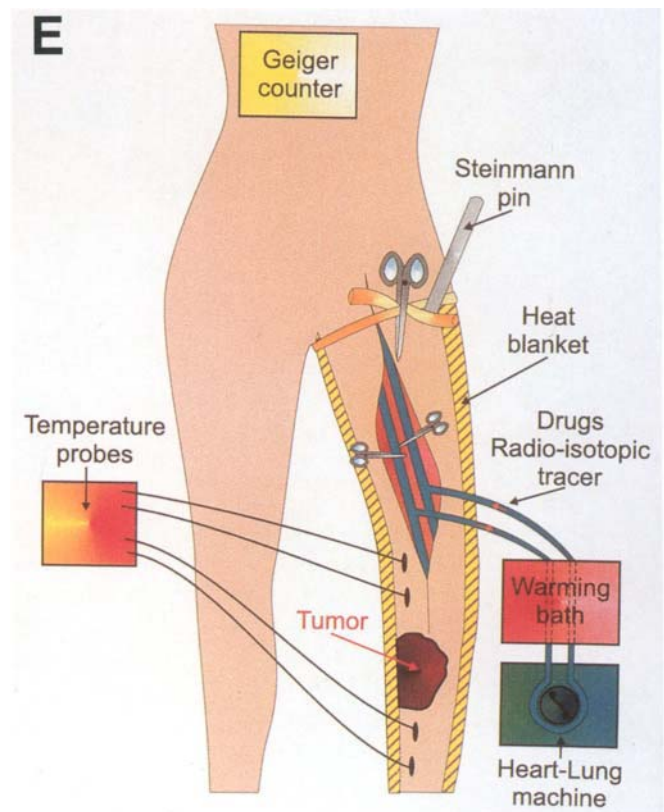


Figure 4.2 Isolated limb perfusion (ILP); stages of the procedure: (A) Entire limb is scrubbed, tissue thermistors are placed; (B) limb is wrapped with heating mattress; (C) wide exposure of the artery and vein, ligation of all the collaterals; (D) cannulation and proximal occlusion of blood vessels; (E) in iliac perfusions, a Steinmann pin is inserted into the iliac bone to anchor the Esmark band.

Rapid shifts in reservoir volume indicate a missed collateral vessel. Rapid leakage also occurs when the cannula or its side holes are placed above the level of the tourniquet. Under such circumstances the pump should be turned off and the operative field re-explored in order to allow identification and ligation of a missed collateral, repositioning of the cannulae, and readjustment of the tourniquet. Less dramatic leakage can be manipulated by reapplication of the tourniquet or adjustment of the circuit flow pressure.

Leakage from the systemic circulation to the limb is less frequent and can usually be dealt with by increasing flow rate or pressure. Systemic leaks of less than 2% can be achieved in almost 95% of patients.^{5,7,8}

This improvement in isolation techniques has made ILP a safe procedure. There is no longer a need for sophisticated, invasive monitoring or intensive care. Patients are routinely transferred to the surgical ward 2–3 h following the procedure.

Termination of ILP

After the drug administration and perfusion treatment periods (e.g. 30 min for TNF alone followed by 90 min of melphalan), the circuit is interrupted and the perfusate washed from the limb with 2 L of saline and 1 L of dextran polymer or blood. The pump is then turned off, the tourniquet cuff is deflated, and the canulae are removed. The vein is repaired and thereafter the arteriotomy is sutured, re-establishing blood flow to the limb.

DRUGS

Melphalan

This alkylating agent, a phenylalanine mustard, was originally selected for melanoma perfusion because phenylalanine is an essential precursor in melanin synthesis and is taken up preferentially by melanocytes.

Melphalan, which is an ideal drug for ILP, possesses a short half-life, low endothelial toxicity, limited cell cycle specificity, and a relatively linear dose–response relationship for cytotoxicity. The optimal dose of melphalan is 10 mg/L limb volume for the lower extremity and 13 mg/L limb volume for upper extremity perfusion. At such dosages, perfusate concentrations of melphalan are 50–100-fold higher than systemic levels, which remain less than 1 $\mu\text{g/ml}$.⁹

Given its high response rate (60–80%) with a complete response of 30–55% in melanoma patients undergoing ILP^{10–12} and the chemoresistant nature of melanoma, it is not surprising that melphalan is the drug of choice for this procedure.

Other Cytotoxic Drugs

Other chemotherapeutic agents, including cisplatin, actinomycin-D, and DTIC, have been tested in conjunction with ILP in both human and animal studies, but none has demonstrated better results than with melphalan.² Cisplatin appears to be suitable for ILP, because its concentration in tumor tissue is selectively increased in the presence of mild hyperthermia. The primary concern is its considerable regional toxicity, especially neurotoxicity. Doxorubicin was also investigated in the ILP setting, mainly for nonresectable STS, but was found ineffective both alone and in combination with melphalan. Regional toxicity was unacceptable, and amputation rates were as high as 40%.¹³

Tumor Necrosis Factor

Tumor necrosis factor- α (TNF- α) was discovered in 1975 and made available for clinical use in 1985.¹⁴ TNF- α can produce very fast and effective tumor necrosis, as has

been demonstrated in a variety of tumor-bearing mice and cultured cancer cells. Attempts to duplicate the effect in humans, however, have failed. Only anecdotal cases of partial response were described in more than 800 cancer patients treated systemically with rTNF- α . This failure was attributed to the inability to administer sufficient doses of TNF because of life-threatening side-effects.^{3,8} Based on data from murine tumor models, the rTNF- α dose required to achieve the antitumor effect is 10–20 times higher than the maximal tolerated systemic dose (MTD) in humans, which is approximately 200 mg/m^2 . Administration of higher doses produces the hemodynamic conditions typically associated with septic shock (e.g., tachycardia, hypotension, decreased vascular resistance, increased cardiac index), as well as coagulopathy, thrombocytopenia, and metabolic impairment such as increased bilirubin and liver enzymes and decreased cholesterol levels.¹⁵ The end result is multiorgan failure. By using rTNF- α in the ILP setting it is possible to overcome barriers raised by the systemic toxicity, and doses of 3–4 mg can be administered.¹⁶

The most pronounced effect of TNF *in vivo* is seen in the tumor's vasculature.⁸ TNF suppresses specific adhesion molecules such as integrin- $\alpha\text{V}\beta 3$ on the surface of endothelial cells within the tumor and on membranal receptors on macrophages and leukocytes.^{17,18} Antagonists of $\alpha\text{V}\beta 3$ interfere with adhesion-dependent signals, causing apoptosis of angiogenic endothelial cells. This TNF-induced endothelial damage is exclusive to tumor vasculature; normal vasculature is spared, as has been demonstrated in angiograms performed in sarcoma patients before and after ILP–TNF.

The administration of TNF alone, as demonstrated in mouse tumor models, human tumor xenografts in nude mice, and a pilot study in six patients, has only a transient antitumor effect. There is regrowth of the tumor after its necrosis.¹⁹ To achieve a high and prolonged response the addition of a cytotoxic drug is mandatory.

Hyperthermia

The fact that heat is effective against cancer and tumor growth has been known since the middle of the nineteenth century. A clinical trial demonstrated a good tumor response to isolation perfusion with a heated perfusate without cytotoxic drugs.² Based on this work, heat was added to the melphalan perfusion system with the general belief that hyperthermic melphalan perfusion is superior to normothermic ILP. Hyperthermia has been the subject of a great deal of research that has led to several hypotheses concerning its role in tumor necrosis. True hyperthermia ($> 41^\circ\text{C}$) decreases the

tissue pH and aerobic glycolysis. It induces cycling of tumor cells and changes the proportion of cells in the sensitive S and M phases. Cell membranes become more sensitive to active agents and the tumor cells, rendering them more vulnerable to cytotoxic drugs. There is an apparent decrease in DNA repair, possibly due to the development of oxygen-free radicals that cause breaks in the DNA strand.

Hyperthermia appears to enhance the antitumoral effect of both TNF and melphalan.²⁰ However, true hyperthermia cannot be used in ILP because of the risk of severe regional toxicity.²¹ Mild hyperthermic conditions, commonly used, are still considered synergistic to melphalan and TNF and do not increase the regional toxicity.²²

COMPLICATIONS OF ILP

Regional Toxicity

The Wieberdink grading system (Table 4.2) is routinely used to evaluate the regional toxic effect of ILP. Mild edema, erythema, discomfort, and a warm limb (grade I) commonly develop within 2–3 days following ILP. Moderate to severe toxicity (grade III–IV) occurs in 15–30% of patients. Patients may develop skin blisters, particularly on the palms of the hand and the soles of the feet. Full-thickness loss is rare. Pain and significant discomfort occur in 25–40% of patients and are probably related to muscle swelling, compartmental syndrome, and neurotoxicity. Limb-threatening complications with extensive tissue injury and severe edema occur in less than 10% of patients. Limb loss occurs only rarely (0.5–1.5%). Most of the complications following ILP resolve spontaneously within 2–3 weeks.²¹

Adding TNF to melphalan, in our experience and that of some others, does not appear to increase regional toxicity.^{8,23} Other groups, however, have reported that the rapid onset, severity, and duration of limb toxicity are more prominent when TNF is added to melphalan. A phase I study revealed that a 6 mg dose of TNF combined with melphalan induced severe muscle and nerve toxicity but TNF alone elicited no regional toxicity.¹⁶

Nerve toxicity, manifested by shooting pain or paresthesias, occurs 2–3 weeks after ILP in 25–40% of patients. It usually resolves within a few months. Long-term neuropathy is rare (1–4%).²¹

Vascular complications may also develop following ILP. Arterial complications are rare and unrelated to the drugs used in ILP. The incidence of thrombosis at the arteriotomy site is 2.5%.²¹

The incidence of DVT is significant (~10%) despite heparinization during ILP. The thrombogenic effect of the tumor, the cytotoxic drugs, and the surgical trauma,

Table 4.2 Regional toxicity – Wieberdink classification

Grade I	No reaction
Grade II	Slight erythema/edema
Grade III	Considerable erythema/edema with some blistering
Grade IV	Extensive epidermolysis and/or obvious damage to the deep tissues, causing functional disturbances; threatening or established compartmental syndrome
Grade V	Reaction which may necessitate amputation

coupled with edema and increased compartmental pressure and decreased mobility, are contributing factors.

Another important category of complications is associated with the rapid necrosis induced by TNF. This is a real threat in patients with ulcerated tumors, in whom an existing bacterial colonization may turn into overt sepsis. Such was our experience with a 14-year-old boy whose ulcerated sarcoma underwent liquefaction necrosis, abscess formation, and uncontrolled sepsis, that necessitated urgent amputation. We also encountered staphylococcal sepsis originating in the infected necrotic tumor that ultimately proved fatal to a 78-year-old patient.

Systemic Side-effects

Most systemic side-effects are caused by leakage of drugs from the perfusate into the systemic circulation during ILP. Even with complete isolation and a thorough wash-out of the perfusate on completion of the ILP, the drug may remain in the tissue of the limb or its intravascular compartment and redistribute once normal systemic circulation is re-established. Systemic toxicity from melphalan perfusion is limited if systemic leakage is less than 10%.²⁴ Since melphalan declines from the perfusate 10 min after administration, its systemic toxicity is mainly related to early leakage. With systemic leakage of melphalan, patients typically experience some nausea and vomiting immediately following ILP. Ten to 14 days later, they develop mild, short-lived neutropenia.

The addition of TNF introduces the risk of immediate life-threatening complications. A stable and high TNF level in the perfusate and limb is present during the entire ILP; consequently, a small but continuous leak may divert a systemically significant dose of TNF. Furthermore, TNF induces the generation of secondary cytokines and mediators, which can elicit many side-

effects, some of which are similar to those observed following rTNF- α administration.⁷

The systemic side-effects of TNF may be divided into three categories: cardiovascular, metabolic, and hematologic.⁵ The most immediate effect involves the cardiovascular system; it manifests by tachycardia, hypotension, increased cardiac index, and a marked decrease in systemic vascular resistance (SVR). Unlike many types of shock, in which vasoconstriction dominates, septic shock associated with TNF leads to a pathognomonic vasodilation. There is good correlation (regression analysis = 0.8) between the severity of the decrease in SVR and the systemic levels of TNF.⁵

Also of importance is the cardiac effect of TNF. Despite the hyperdynamic state and increase in cardiac index associated with the drug, it produces an overall cardiodepressant effect, which manifests by a decrease in the left ventricular stroke work index. The metabolic effects of TNF mainly relate to hepatic toxic effects and may include hyperbilirubinemia, increased levels of liver enzymes, and marked hypocholesterolemia. The hematologic systemic side-effects are manifested by leukopenia, thrombocytopenia, and coagulopathy.

With the standardization of the ILP technique and meticulous isolation, systemic leakage is minimized. This virtually eliminates side-effects and greatly simplifies the entire procedure. No special monitoring and intensive care are required, and the patient may be transferred to the surgical ward 2–3 h following the procedure.

ILP FOR EXTREMITY SOFT-TISSUE SARCOMA

As it became evident that amputation is not mandatory in patients with soft-tissue sarcoma, and that comparable survival rates can be achieved with adequate tumor resection,²⁵ limb preservation became a major goal. However, when the tumor is large, expanding into more than one compartment, or it is adjacent to or invading a major blood vessel or nerve, or when there is a multifocal appearance, amputation or mutilating surgery are still considered almost inevitable.

Several treatment modalities have been developed to facilitate limb-sparing in patients with advanced tumors. Neoadjuvant therapies, mainly preoperative radiation or a combined preoperative (intra-arterial and/or systemic) chemo- and radiotherapy^{26,27}, have led to a significant reduction in amputation rates (which were 50% prior to 1977), although 8–15% of patients with extremity sarcoma still undergo amputation.²⁶

Prior to the era of TNF-based perfusion, ILP was not a viable option for tumor reduction in STS due to poor response rates.²⁸ However, promising results following the introduction of high-dose TNF in ILP³ led to a

phase II multicenter study to determine the effect of ILP with TNF and melphalan in patients with nonresectable STS confined to the limb. Because resection is impossible, amputation is almost always necessary in this group.

ILP/TNF is also indicated as a palliative measure in selected patients who have a reasonable life expectancy in the presence of distant STS metastasis. In these cases, avoidance of amputation is the main goal.

The typical changes following ILP/TNF may be summarized as follows:

- In large, bulky tumors, marked softening can be noticed in the first days post-ILP, but this is not an accurate measurement for response because it may be secondary to edema following perfusion.
- The tumor mass may become smaller or completely disappear both clinically and on imaging studies. At times the mass reduction is limited, but in cases where the tumor is adherent to a major nerve (e.g. sciatic nerve) or blood vessel (e.g. popliteal vessels), even a small change in size (e.g. 2–3 cm), can make it possible to perform marginal resection and to preserve these structures.
- In ulcerated tumors that penetrate the skin, hemorrhagic necrosis can be seen even a few hours after the perfusion.

An accurate assessment of response in STS following ILP/TNF is difficult. The disappearance of the vascular bed, as demonstrated by postoperative angiography, is usually a good indicator of massive necrosis. Newer techniques, such as magnetic resonance spectroscopy and positron-emission tomography scanning,^{29,30} can be useful in assessing the extent of necrosis vs. tumor viability and increase the accuracy of response assessment.

Histopathology is the most accurate method with which to assess tumor response. Typical histological changes 6–8 weeks after TNF perfusion include cystic hemorrhagic necrosis in the central area of the remaining tumor. Although spontaneous necrosis is encountered in STS, the magnitude and extent of necrosis following ILP/TNF are unique. If any viable tumor cells exist, they are usually observed in the periphery of these "cysts" but their malignant potential cannot be fully determined. Other histological changes are extensive interstitial and pericystic fibrosis, which can also be seen following neoadjuvant chemotherapy. No correlation has been found between tumor size, histological subtype, and pattern of response.

There is a notable discrepancy between the clinical and the pathological response assessments. A histological examination can upgrade the overall

response rate, since masses that remain unchanged or only partially regressed may be converted into a complete response (no viable tumor cells) following pathological examination. Since studies performed on sarcoma patients undergoing ILP with cytostatic drugs in the pre-TNF era were based only on clinical and radiological assessment, the reported response rates may have been underestimated relative to pathologically based TNF studies.

Result of ILP/TNF in STS

A review of worldwide experience with ILP using rTNF- α and melphalan \pm IFN (Table 4.3) discloses an overall response rate of 82–100%, with a complete response of 29–67% and partial response of 22–56%. Eighteen percent or less of patients exhibited no response or a progression of disease. In 20% of patients with a partial response, a near-total response ($> 95\%$ necrosis) was found. Only the finding of several tumor cells precluded categorizing these patients as having a complete response.^{8,16,23,31}

These results were obtained in a selected group of patients with very extensive disease. All were candidates for amputation. The average tumor size was 16cm; most tumors were high-grade (85%), and 43% were recurrent.^{8,23} There was also a relatively high rate of multifocal disease (23%). In this group of patients, who have a grave prognosis anyway, the value of limb preservation is even more enhanced.³²

Limb salvage has been achieved in 85% of these patients. This high rate is the most valuable and proven benefit of ILP/TNF in advanced sarcoma patients. Complete response *per se* is not crucial; whether the tumor responds completely or partially is irrelevant, as

Table 4.3 ILP/TNF + melphalan in STS

Author	Ref.	Year	Drug	No. of patients	% RR	% CR
Vaglini	31	1994	TNF + melph	9	89	67
Gutman	23	1996	TNF + melph	35	94	37
Eggermont	8	1996	TNF/melph/TNF- γ	186	82	29

long as it becomes amenable to resection without loss of limb function.

A tumor that has shrunk considerably may still be impossible to resect without endangering limb function. In such cases a second perfusion may be considered to achieve further tumor shrinkage. Our experience with nine PR patients with very large tumors who underwent two TNF perfusions scheduled 6–10 weeks apart, resulted in the conversion of six to complete response and two to further tumor shrinkage. Limb salvage was ultimately possible in eight of these patients.

The response to ILP/TNF is remarkable, but is it longstanding? Recurrent local disease in patients whose limbs are considered salvages after ILP/TNF ranges from 10% to 15% after 3–24 months (median follow-up 22 months).^{8,23} This recurrence rate is relatively low, considering the large median tumor size, the percentage of recurrent sarcomas (40%), and the large percentage (25%) of multifocal STS in this group. Local recurrence rates could probably be further improved by the administration of postresection radiation therapy to a higher percentage of patients.

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The Role of Radiation Therapy in the Treatment of Bone and Soft-tissue Sarcomas

Brian G. Fuller

INTRODUCTION

The role of radiation therapy in the management of soft-tissue and bone sarcoma has changed over the past 40 years and it continues to evolve. Radiotherapy is currently accepted as a standard adjuvant for most soft-tissue sarcomas of high grade, while the routine use of adjuvant radiotherapy for low-grade sarcomas is controversial. Preoperative chemotherapy has largely replaced radiotherapy in the local management of osteosarcoma.

There were several reasons for the initial belief that sarcomas were radioresistant. Until the 1960s megavoltage radiation beams were not generally available, and successful treatment of bulky, often deep-seated sarcoma was limited by the poor depth of penetration of lower-energy orthovoltage beams.^{1,2} Historically, single-modality treatment (surgery or radiation) was often employed to treat tumors which more frequently were allowed to reach large size prior to medical intervention. Finally, the previously held belief, that the rate of clinical regression was a measure of radiocurability, is no longer considered valid.

It is now recognized that tumors are often composed of dense stroma containing blood vessels, connective tissue, and mucinous or osteoid matrix, and that these elements may resolve slowly after sterilization of malignant cells. With the observation that radiotherapy is most successful when used to eradicate microscopic extensions of tumor, it became clear that routine application of adjuvant radiation could allow reductions in the volume of resected "normal tissue", and permit limb-sparing procedures to be utilized without significant reductions in local control or disease-free survival.^{3,4} Contemporary issues which remain unresolved pertain to the timing and volume of adjuvant radiotherapy for soft-tissue and Ewing's sarcoma, and to the identification of more effective systematic therapy for soft-tissue and bone sarcoma.

RADIOBIOLOGY

Contrary to previous beliefs, clonogenic survival assays of human soft-tissue sarcoma and bone sarcoma cell lines reveal no consistent evidence of intrinsic resistance to radiation. The surviving fraction at 2 Gray (SF₂) has been accepted as a clinically relevant measure of radiation sensitivity. Ruka *et al.*,⁵ Mundt *et al.*,⁶ and Dahlberg⁷ evaluated SF₂ values in carcinoma, sarcoma, and normal fibroblast cell lines. The average SF₂ value for sarcoma was 0.24 (summarized in Table 5.1). Although the tumor cells which had the highest SF₂ values in the Mundt analysis also developed local recurrence, SF₂ values for sarcoma were lower than those for squamous carcinoma, and were not different from SF₂ values for normal fibroblasts.⁵⁻⁷ In addition, the radiation dose required to locally control breast and squamous carcinomas following complete resection is identical to the dose required for local control of soft-tissue sarcoma. These observations suggest that the alleged "radioresistance" of sarcomas is without basis (see Figures 5.1 and 5.2).

RESULTS OF LOCAL TREATMENT OF SARCOMA

Soft-tissue Sarcoma

Surgery Alone

In highly selected patients, wide excision alone produces excellent local control rates (90% and higher, see Table 5.2). Criteria used to select patients for wide excision alone include: size less than 5 cm, superficial location, confinement within one fascial compartment, and resection margins $\geq 1-2$ cm. Berlin and colleagues reported 137 patients treated with surgical resection without adjuvant radiation therapy to the primary site. Local control was achieved in 89% of resected patients with radical or wide margins, compared to only 34% of patients with "marginal" margins ($p = 0.05$). Multivariate analysis identified advanced age, open biopsy, and marginal resection as predictors of local recurrence.⁸ In a later report from Sweden by Rydholm *et al.*, limb-sparing surgery alone produced local control in 52 of 56

(92%) patients. In this report, sarcomas in the subcutaneous tissues were resected with a cuff of uninvolved fat and the layer of deep fascia below the tumor. Intramuscular tumors were treated with resection alone if there had not been an open biopsy, and if the undisturbed tumor could be removed via myectomy or limited (one muscle) compartmental resection. The principles of diagnostic evaluation and surgical resection described by Rydholm *et al.* in this report are informative and warrant review.⁹

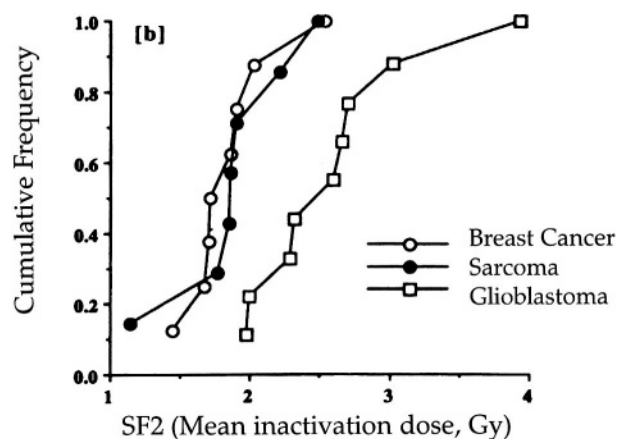
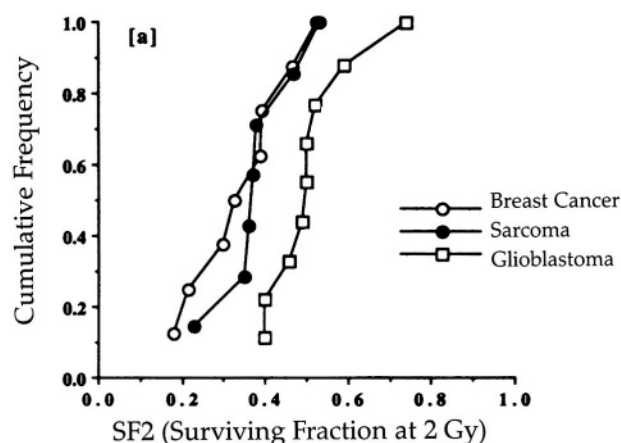


Table 5.1 Radiobiologic parameters of soft-tissue sarcoma

Reference	Sarcoma cell lines	Mean inactivation dosage	Mean SF ₂
Ruka <i>et al.</i> ⁵	7	120	0.39
Mundt <i>et al.</i> ⁶	13	115.7	0.26
Dahlberg <i>et al.</i> ⁷	12	90.1	0.124
Total	32	107	0.24

cGy = centigray; SF₂ = positron.

Figure 5.1 A comparison of radiosensitivity among sarcoma, breast cancer and glioblastoma cell lines as determined in Figure 5.1A by the surviving fraction at 2 Gy (SF₂), and in Figure 5.1B by the mean inactivation dose. These data demonstrate no difference in inherent radiosensitivity parameters between breast cancer and soft-tissue sarcoma cell lines as determined in the colony formation assay. Although the *in-vitro* parameters do not predict clinical responses, the doses used to successfully treat breast cancer are very similar to those used to locally control soft tissue sarcoma (from ref. 5).

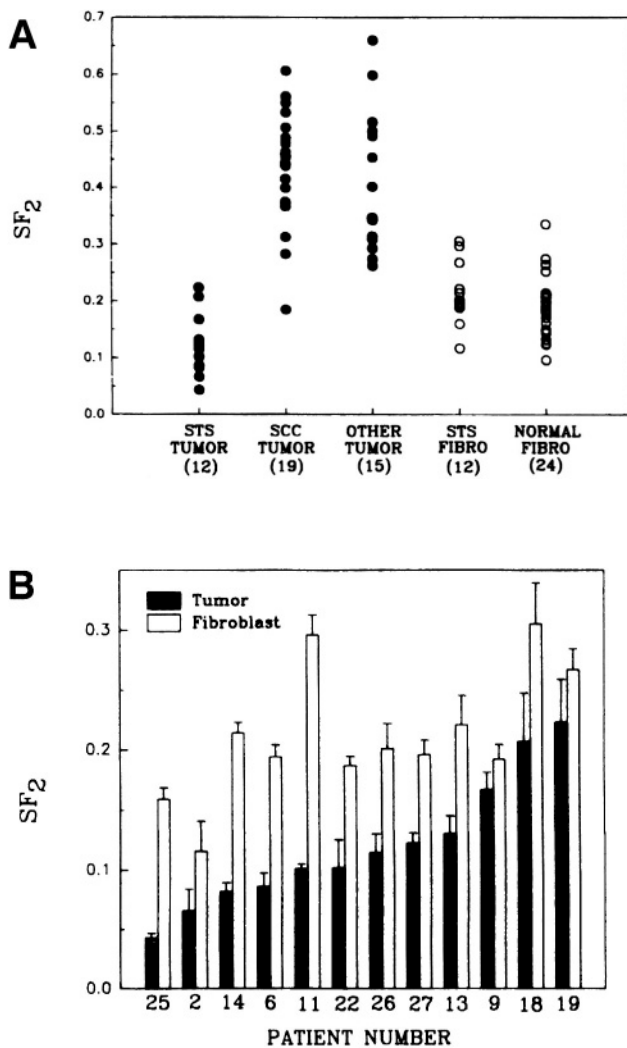


Figure 5.2 A comparison of the surviving fraction at 2 Gy (SF_2) values for soft-tissue sarcoma cell lines and several other cell types. In Figure 5.2A soft-tissue sarcoma (STS) tumor cell lines are compared to squamous cell carcinoma (SCC) cell lines, various other tumor cell lines, syngeneic fibroblast (STS Fibro) cell lines, and fibroblast cell lines from normal volunteers (Normal Fibro). These data demonstrate that there is no inherent radioresistance in STS cell lines. In Figure 5.2B a comparison is made of the radiosensitivity of STS cell lines and syngeneic normal fibroblast strains from the tumor-bearing host. Note the consistently more radiosensitive phenotype among tumor cell lines compared to normal fibroblasts from the same host. Patients number 11 and 27 represent lymphoma cell lines (from ref. 7).

Excellent local control following surgery alone in selected patients was also reported by Karakousis and co-workers. Of 152 patients reviewed, 143 (94%) had a limb-sparing procedure. Local control was achieved in 90% following surgery alone. For grade II and grade III tumors, local control was 88%.¹⁰ Geer *et al.* reported

Table 5.2 Wide local excision alone for soft-tissue sarcoma

Reference	No. of patients	Locally controlled	Percent
Markhede (1982)	63	58	92
Berlin (1990)	76	66	87
Rhydhalm (1991)	56	52	93
Geer (1992)	117	106	90.6
Karakousis (1995)	107	95	89
Gibb (1997)	35	35	100
Baldini (1999)	74	70	94.6
<i>Total</i>	528	482	91

excellent local control and survival for soft-tissue sarcoma < 5 cm in diameter following limb-sparing resection. The 5-year actuarial local disease-free survival following surgery alone was 92%. Multivariate analysis revealed only age > 50 years as a predictor of local recurrence.¹¹

Most recently, Baldini *et al.* reported 74 patients with primary, nonmetastatic soft-tissue sarcoma of the extremity or trunk who were treated with function-sparing surgery and no radiation. Sixty patients had wide excision (1–2 cm margin of adjacent normal tissue), 13 patients had radical excision (entire muscle compartment), and one patient had a marginal excision. Sixty-eight (92%) had negative margins, five (7%) had microscopically positive margins and one patient had a grossly positive margin. Only four of the 74 patients developed local failure, for a local control rate of 95%. The actuarial rates for local control at 5 and 10 years are 96% and 93%, respectively. The only factor identified as a predictor of local recurrence was surgical margins less than 1 cm.¹² From these and other reports,^{13,14} it is clear that selected subsets of patients can be treated with function-sparing resection alone. In the Swedish⁹ and Brigham and Women's/Dana Farber¹² experiences, this constitutes approximately 30% of patients who present with soft-tissue sarcoma. Guidelines for the selection of patients for limb-sparing resection alone are listed in Table 5.3.

Radiation Alone

Analogous to observations regarding epithelial tumors > 5 cm in diameter, radiation alone is rarely adequate to produce durable local control of soft-tissue sarcoma. Normal tissue radiation tolerance often prohibits the radiation of bulky tumors to dose levels required for sterilization. Leibel *et al.* reported five patients with intermediate or high-grade tumors > 5 cm in diameter who were treated with radiation alone. None were locally controlled.¹⁵ Tepper and Suit reviewed the

Table 5.3 Selection factors for considering surgery alone for sarcoma

	Yes	Possibly	No
Size	<5 cm	5–10 cm	>10 cm
Margins	>2 cm	1–2 cm	≤ 1 cm
Biopsy	FNA	Trucut	Open biopsy
Primary vs. recurrent	Primary	Recurrent, new site	Recurrent, old site
Fascial investment	Complete	Partial	Involved
Previous surgery	No	Yes	Complete resection
Grade	I	II–III	—
Age	<50	—	>50

Massachusetts General Hospital experience with radiation alone for soft-tissue sarcoma. Patients were treated from 1971 to 1982 using megavoltage equipment to total doses of 64–66 Gy. Forty-four of 51 patients were evaluable with > 5 years follow-up. The 5-year local control rate was 33%. Local control for tumor ≤ 5 cm was 87%, for tumors 5–10 cm it was 53%, and for tumors >10 cm it was 30%. Total doses equivalent to <64 Gy were associated with poor local control.¹⁶ Thus, conventional photon radiation alone will be unsuccessful in controlling the majority of soft-tissue sarcomas >5 cm. However, palliation of symptoms and the possibility of local control can be offered to patients who refuse resection, or who are surgically unfit. Distant metastases in patients with large high-grade tumors pose the greatest limitations on survival. The results of radiotherapy alone for soft-tissue sarcoma from various series are summarized in Table 5.4.

The Role of Radiotherapy in Limb Salvage for Soft-tissue Sarcoma

Early recognition that wide local excision (WLE) of high-grade sarcomas resulted in unacceptably high rates of local failure (20–70%),^{17,18} led surgical oncologists of the 1950s and 1960s to advocate amputation as the procedure of choice.¹⁸ With the development of megavoltage radiation beams in the 1960s, bulky, deep-seated tumors could be treated to high doses with relative sparing of skin and subcutaneous tissues. In the mid-1970s several institutions initiated clinical trials evaluating WLE combined with preoperative or postoperative radiation and chemotherapy. The goal of these studies was preservation of a useful, functioning limb.

Table 5.4 Radiation alone for soft-tissue sarcoma

References	No. of patients	Local control	Year
McNeer <i>et al.</i> ¹⁹	25	14/25 (56%)	1968
Suit <i>et al.</i> ²¹	18	15/18 (83%)	1975
Leibel <i>et al.</i> ¹⁵	5	0%	1982
Tepper and Suit ¹⁶	5 (<5 cm) 17 (≥ 5–10 cm) 10 (≥ 10 cm)	87% 53% 30%	1985

Retrospective analyses published in the late 1960s and early 1970s from Memorial Hospital in New York and MD Anderson Hospital suggested that acceptable local control rates could be achieved when a less than radical resection was combined with radiotherapy. McNeer *et al.* reported the Memorial Hospital experience from 1935 to 1959 in which 653 patients with soft-tissue sarcomas were treated with curative intent. Twenty-five were treated with radiation only, 46 received preoperative radiation, 96 received postoperative radiation and 486 received surgery only. A variety of radiotherapy techniques were used including orthovoltage, radium packs, cobalt 60, high-energy electrons and megavoltage photons. Total doses ranged from 1500 to 7000 rad; however, most patients received >3000 rad. From 1935 to 1945 radiation was routinely administered. From 1946 onward radical resection, including amputation, was emphasized. Patients with bulky tumors received preoperative radiotherapy to facilitate resection. During this period postoperative radiotherapy was given if it was felt that the margins of excision were close or positive. Radiotherapy alone was reserved for patients who refused surgery or who were medically inoperable. Local control was 75% following surgery alone, 56% following radiation alone, 63% following preoperative radiation, and 66% following postoperative radiotherapy. It was noted by the authors that patients with the less favorable prognoses received radiotherapy. The clinical response rate of 72% and the histologic complete sterilization rate of 33% produced by radiotherapy, prompted the authors to recommend routine preoperative radiotherapy in 1968.¹⁹

From 1961 to 1969, 57 patients with soft-tissue sarcomas who were recommended to receive amputation were treated by Suit and colleagues at MD Anderson Hospital with radiotherapy alone or combined with simple excision. Twenty-seven patients were treated with conventional fractionation and 30 patients were treated with high-dose radiotherapy and tourniquet-induced hypoxia. Local control was achieved in 87% (50/57). Thirteen patients (23%) required amputation.

Six patients treated with very high-dose radiotherapy (12,000–14,000 rad) and "tourniquet technique" required amputation for severe radiation toxicity. The remaining amputations were performed for persistent or recurrent disease (seven patients). Many patients were treated with grossly positive margins or with palpable tumor.²⁰ Several refinements in radiotherapy treatment technique emerged from these early experiences, such as avoidance of circumferential irradiation of limbs, the use of progressively smaller volumes of irradiation exposure (i.e. "shrinking-field" technique), and minimization of normal tissue exposure through complex field arrangements.^{20,21} In an update of this series, the results of 100 patients were reviewed. Local control was achieved in 87%. Seventy-five percent of patients retained a useful limb, and overall local control rates were similar to those achieved with amputation.²²

Data from these and other institutions strongly suggested that alternatives to amputation, such as limited surgical resection and carefully planned radiotherapy produced good local control rates and offered the possibility of preserving a functioning limb. Results from several early series are summarized in Table 5.5. While these studies disproved the myth of "radio resistance" which surrounded soft-tissue sarcomas, non-controlled retrospective series did not allow meaningful comparisons of radical surgery to limb-sparing surgery and radiotherapy. Prospective randomized trials were needed.

In May of 1975 the National Cancer Institute initiated a prospective randomized trial of radical surgery (amputation) and chemotherapy versus limited surgery, radiation and chemotherapy. Sixteen patients were randomized to receive amputation. There were no local recurrences in this group. Twenty-seven patients received limited surgery and postoperative radiation. There were four recurrences in the conservative surgery group (local recurrence rate = 15%). The difference in local recurrence rates was of borderline significance. There was no difference in disease-free or overall survival between these two groups (results are summarized in Table 5.6).³

In an update of their experience reported by Potter *et al.* in 1986, local control following amputation and chemotherapy remained 100% (0/83 local failures), and local control following WLE and postoperative radiotherapy with or without chemotherapy was 92% (12/128) local failures. In this latter analysis of the randomized NCI studies of soft-tissue sarcoma, the use of adjuvant chemotherapy was associated with improved local control in patients who were treated with limb-sparing surgery and radiotherapy.²³ The contribution of chemotherapy to local control has recently been described for head and neck, and truncal

Table 5.5 Surgery plus postoperative radiation for soft-tissue sarcomas – early results

Reference	No. of patients	Local control	Year
McNeer <i>et al.</i> ¹⁹	94	62/94 (66%)	1968
Spittle <i>et al.</i> ²⁷¹	49	38/49 (80%)	1970
Suit <i>et al.</i> ²⁰	57	50/57 (87%)	1973

Table 5.6 Results of the NCI randomized trial of limb preservation: amputation versus resection and radiation³

Amputation	Limb preservation	p-Value
Sixteen patients	Twenty-seven patients	
Local control = 100%	Local control = 85%	0.06
Disease-free survival = 78%	Disease-free survival = 71%	0.75
Overall survival = 88%	Overall survival = 83%	0.99

sarcomas treated in a European randomized trial,²⁴ and is relevant when reviewing the most recent results reported from the NCI.⁴

After the seminal reports by McNeer, Suit, Lindberg, and Rosenberg and co-workers^{3,19,20,21,25} which demonstrated that amputation could be avoided without significant reductions in local control or survival, postoperative radiotherapy was accepted as standard following WLE or limb salvage surgery for high-grade soft-tissue sarcomas. A number of reports from America and Europe have documented the success of WLE and postoperative radiotherapy. Local control in these reports ranged from 80% to 100%, which are summarized in Table 5.7.^{4,6,23,25–32}

Prognostic Factors for Local Control following Surgery and Postoperative Radiation

Although agreement exists that there is excellent local control following WLE and radiotherapy, a number of issues remain controversial regarding prognostic factors. Several of these prognostic factors are listed in Table 5.8 and discussed briefly below.

Age

Age at diagnosis has been reported as a predictor of local control. Several multivariate analyses of prognostic factors which address local recurrence have been published by investigators at Memorial Sloan Kettering Cancer Center from 1988 to 1996.^{11,33–35} In each of these, age >50 years (53 years in the report by Collin *et al.*³³)

Table 5.7 Results of limb preservation with excision and radiation for soft-tissue sarcoma

Reference	No. of patients	Local control
Yang <i>et al.</i> ⁴	70	69/70 (98.6%)
Wilson <i>et al.</i> ²⁷	62	59/62 (95%)
Dinges <i>et al.</i> ²⁸	102	84/102 (82%)
Keus <i>et al.</i> ²⁹	117	99/117 (85%)
Fein <i>et al.</i> ³⁰	67	61/67 (91%)
Cakir <i>et al.</i> ⁴¹	75	50/75 (67%)
Pao and Pilepich ⁴⁷	50	39/50 (78%)
Mundt <i>et al.</i> ⁶	64	53/64 (83%)
Lindberg <i>et al.</i> ²⁵	300	233/300 (78%)
Total	907	727/907 (80%)

Table 5.8 Prognostic factors for local control following surgery and postoperative radiation

Factor	Predictive value	Supported (references)	Not supported (references)
Age	Controversial	8, 11, 33–38	23, 29, 39–45
Histology	Controversial	21, 25, 32, 34	4, 7, 23, 32, 40, 41
Grade	Controversial	10, 15, 20, 25, 28, 29, 33, 42, 47	23, 30, 34, 48
Location	Established*	20, 21, 25, 35, 38, 42, 51, 52	23, 28, 29, 32–34, 43, 44, 48, 53 [†]
Depth	Controversial	29, 42	33, 34, 45, 47, 53, 54
Size	No predictive value	21	21, 23, 28–33, 35, 41, 43, 44, 53, 55
Margins	Established	29, 31–33, 37, 41, 43–45, 47, 48, 49, 53, 56, 58, 59, 62	4, 23, 24
Recurrent tumor	Established	28, 31, 33–35, 40, 43, 44	29, 37
Radiotherapy target volume	Suggestive	6, 48	29
Radiation dose	Suggestive	28, 30	29, 41

*Tumor location is a significant predictor of local control when different major anatomic sites are compared (i.e. extremity versus retroperitoneum).

[†]When different locations on an extremity are compared there is no predictive value.

was identified as an independent predictor of local recurrence following conservative surgery and radiotherapy. The underlying biologic explanation for this finding is not discussed in these reports, which have been recently reviewed.³⁶ Similar results were reported by Swedish investigators in 1982 and 1990.^{8,14} In the earlier report, more advanced age was associated with local recurrence. However, when the model was corrected for the adequacy of surgical resection, age lost its prognostic significance.¹⁴ Such a correction for interdependent variables was not discussed in the later report, despite the fact that patients diagnosed with malignant fibrous histiocytoma tended to be older than patients with other histologic types.⁸

Younger age was predictive of better local control in a multivariate analysis reported from the Princess Margaret Hospital. However, an explanation for this finding, and its implications for patient management were not offered.³⁷ More recently a report from the Danish Center for Bone and Soft Tissue Sarcomas described 316 patients with truncal and extremity sarcomas. Age >56 years was associated with increased local recurrence, and decreased survival. However, of the 316 patients reviewed, only 50 received adjuvant radiotherapy.³⁸ Age had no impact on local recurrence in multivariate analyses in nine other reports, including those from the NCI/NIH, MD Anderson, the French Federation, and Harvard Medical School.^{23,29,39–45} It thus appears that for local control following conservative surgery and radiotherapy, the significance of age >50 years remains unexplained and controversial. However, age should be taken into consideration if the wide excision alone without radiotherapy is being contemplated. In this setting age >50 has been associated with local recurrence.^{8,38}

Histology

Several authors have described higher local failure rates following conservative surgery and radiotherapy for various histologic types. Lindberg *et al.* reported higher local failure rates for neurofibrosarcomas than for liposarcoma.²⁵ Higher local failure rates for non-liposarcoma was also noted by Herbert *et al.*³² Suit *et al.* described a higher frequency of local recurrence for neurofibrosarcomas and malignant fibrous histiocytoma when analysis was limited to large tumors.²¹ Angiosarcoma, malignant peripheral nerve sheath tumors and embryonal rhabdomyosarcoma were associated with an increased risk of local recurrence in comparison to liposarcoma, fibrosarcoma and non-embryonal rhabdomyosarcoma in a review of prognostic factors for local recurrence from Memorial Sloan Kettering.³³ In a more recent analysis of prognostic factors in 1041 patients from Memorial Sloan Kettering,

malignant peripheral nerve sheath tumor histology emerged as an independent prognostic factor for local recurrence and lower disease-specific survival.³⁴ Other institutions have not been able to identify histologic type of sarcomas as an independent predictor of local failure.^{4,7,23,31,40,41}

Grade

Following WLE alone, the risk of local recurrence increases, and the time to local recurrence decreases, with increasing histologic grade.⁴⁶ Although grade clearly impacts disease-free and overall survival, the influence of tumor grade on local control following postoperative radiation is not without controversy. Most authors describe superior local control for grade I tumors in comparison to grade II or grade III sarcomas.^{10,15,21,25,28,29,33,42,47} Suit *et al.* reported 0/23 local recurrences for grade I sarcomas versus a 17% local recurrence rate for grade II and III lesions following resection and postoperative radiation.²¹ Lindberg *et al.* reported significantly fewer local recurrences among grade I tumors.²⁵ Zero local recurrences for grade I sarcomas following excision and postoperative radiation have been reported from several centers.^{7,10,15} Multivariate analysis of factors affecting local control identified tumor grade as an independent predictor of local recurrence in series from Germany, France, the Netherlands, Canada and Memorial Sloan Kettering.^{28,29,33,42,47} However, reports from Fox Chase Cancer Center and the Malinkrodt Institute of Radiology fail to identify grade as a factor prognostic for local control.^{30,48} Indeed, in a multivariate analysis reported by Potter *et al.* from NCI, and in an updated multivariate analysis by Pisters *et al.* from Memorial Sloan Kettering, tumor grade was not identified as a predictor of local control.^{23,34} It is conceivable that differences in the surgical policies for WLE and/or duration of follow-up might explain the conflicting data regarding the impact of tumor grade on local control. This controversy is compounded by the observation that local control following resection and brachytherapy was less favorable in low-grade tumors treated at Memorial Sloan Kettering^{48,49} (see below). Although by no means a settled issue, it appears that the rate of local recurrence following conservative surgery and radiation appears to increase with increasing grade; and the increase in local recurrence for high-grade tumors can be reduced by more aggressive treatment (i.e. more extensive surgery, the use of adjuvant chemotherapy).

Location/Depth

Tumor location has been shown to affect local control, risk of metastases and survival.^{35,38} Retroperitoneal

tumors have by far the worst local failure rates and are associated with the poorest survival.^{42,50–52} Lindberg *et al.* described significantly fewer local recurrences for primaries of the upper extremity compared to those in the abdomen.²⁵ Coindre *et al.* reviewed prognostic factors for 546 patients with soft-tissue sarcomas, 57% of which received postoperative radiotherapy. Local recurrence-free survival was greater for tumors arising in a limb compared to tumors arising in retroperitoneal, intra-abdominal and pelvic sites.⁴²

The prognostic importance of tumor location on the extremity has been reported by several investigators. Suit *et al.* found that distal location in an extremity (i.e. at or below the elbow or knee) was associated with improved local control.^{20,21} Others have found no association between tumor site on the extremity and local control.^{23,28,29,32–34,43,44,48,53}

Although tumor depth has been reported by several investigators to impact disease-free and overall survival,^{29,33,36,42} less attention has been focused on the implication of tumor depth for local control. Tumor depth was of borderline significance in predicting local control in a series of 156 patients from the Netherlands Cancer Institute.²⁹ In a multivariate analysis of 546 patients from the French federation of cancer centers sarcoma group, Coindre and co-workers reported that deep tumors were associated with higher local failure in univariate, but not multivariate analysis. In that analysis, significantly more patients with deep tumors received postoperative radiation than did patients with superficial tumors, underscoring the importance of radiotherapy in controlling deep soft-tissue sarcomas.⁴² However, tumor site and depth are often interdependent with other prognostic factors, as was shown by Mandard *et al.* Superficial site was linked to other favorable prognostic factors such as small tumor size, intercompartmental location, adequate excision and absence of necrosis or blood vessel invasion. Deep location was linked to large tumor size, extracompartmental tumors, incomplete excision and high mitotic rate. When adjustment was made to correct for independent variables, tumor depth was no longer an independent variable.⁴⁵ Peabody *et al.* evaluated the prognostic importance of tumor depth in patients with soft-tissue sarcomas. Local recurrence was seen in 1/52 superficial tumors and 8/120 deep tumors. A Cox proportional-hazards model revealed that tumor depth was not a significant prognostic factor. However, tumor size and grade were significant prognostic factors.⁵⁴

Gaynor *et al.* found deep location to be a prognostic factor for local recurrence in a univariate analysis. However, deep location was significantly associated with inadequate surgical margin, which was a significant predictor of local recurrence in a Cox analysis.³⁵ Indeed,

several multivariate analyses have failed to identify tumor depth as a significant independent prognostic factor for local control.^{33,34,47,53}

Size

Tumor size and grade are important predictors of metastatic risk and survival. However, the importance of tumor size in obtaining local control is, at best, less certain. Tumor size is less likely to be important for local control with meticulous surgical and radiotherapy technique. Suit *et al.* reported an 8% local recurrence frequency for tumors <5 cm compared to 18% in tumors >5 cm, although this difference was not significant.²¹ In an additional 13 reports, size was not important in predicting local failure following resection and postoperative radiation.^{23,28–33,35,41,43,44,53,55} Thus tumor size appears not to be independently predictive of local recurrence with adequate surgery and postoperative radiation.

Margins

The pathologic margin is one of the most powerful predictors of local failure following surgery and postoperative radiotherapy of soft-tissue sarcoma. Despite this fact there are no uniformly applied standards for analysis or reporting of the status of resection margins. Reported results range from subjective assessments of the adequacy of resection⁵⁵ to the "visualization" of gross disease at the time of surgery, to actual histopathologic assessments described in pathologic reports.⁵⁶ The non-uniformity in the pathologic reporting of soft-tissue sarcomas has resulted in the proposal of a minimum set of voluntary guidelines.⁵⁷

Pao and Pilepich reported 50 patients treated with resection and postoperative radiotherapy at the Malinkodt Institute of Radiology.⁴⁷ All 11 patients who developed local recurrence had gross residual disease or positive margins. In a subsequent report from that institution, Fagundes *et al.* obtained local control in 91% (9% local failure) of patients with negative margins, compared to only 61% (39% local failure) of patients with positive margins.⁵⁸

Bell *et al.* analyzed results of 100 patients treated at Princess Margaret Hospital in Toronto with surgical resection and postoperative radiotherapy. They found that the only factor independently predictive of local recurrence was whether the surgical margin was positive ($p = 0.0004$).⁵⁹ In a subsequent report from Princess Margaret, LeVay *et al.* demonstrated that the rate of recurrence increases following WLE and postoperative radiation with increasing amounts of residual tumor. The recurrence rate for negative margins was 7%, for close margins 17%, for microscopically positive margins 22%, and for grossly

positive margins 77%. Grossly positive margins was the only independent predictor of local failure in multivariate analysis ($p = 0.001$).³⁷

Positive margins, or incomplete resections, have been identified as predictors of local recurrence following conservative surgery and postoperative radiation in more than a dozen reports.^{29,31–33,40,41,43–45,47,48,53,56,58,59} However, several reports failed to detect an influence of surgical margins on local control when adjuvant chemotherapy was given for high-grade sarcoma.^{4,23,24}

An inadequate initial operation for an unsuspected malignant sarcoma is a frequent cause of positive margins or incomplete resection. Giuliano and Eilber reviewed 90 patients referred to UCLA following initial unplanned excision of soft-tissue sarcoma. Microscopic residual tumor was found in 45% of re-excision specimens following initially inadequate surgery.⁶⁰ Zoring *et al.* reported residual tumor in 45% of re-excision specimens following initially inadequate surgery.⁵⁶ Noria *et al.* identified residual disease in 35% of patients following unplanned excision. They could not identify factors which could be associated with an increased risk of residual disease following initial unplanned resection.⁶¹ Karakousis *et al.* found residual microscopic tumor in 91% of re-excision specimens in patients initially referred with "complete" excisions.¹⁰

Radiotherapy has been shown to reduce the risk of local recurrence following an initial inadequate surgery, and it improves local control in the setting of positive margins following re-excision.^{56,60} Liebel *et al.* demonstrated that 22 out of 23 patients undergoing conservative surgery and radiation had positive microscopic margins or small amounts of residual disease, and only 3/22 (14%) developed local recurrence compared to 12/16 (75%) nonirradiated patients with residual disease following conservative excision.¹⁵

Positive resection margins reduce local control following excision and postoperative radiation by 18–64% (average 32%).^{30–32,34,41,43–45,47,53,55,58,59} Whenever possible, re-excision should be performed to achieve negative margins. Re-excision is particularly important in the setting of an unplanned excision of a malignant sarcoma. In this setting the risk of residual disease is at least 40–50%, and post-re-excision radiotherapy can reduce the risk of local recurrence by 9–60%.^{15,56} Davis *et al.* analyzed 239 patients with soft-tissue sarcomas who received excision and radiotherapy. One hundred and four patients presented after an unplanned excision of sarcoma and then had re-excision of the surgical site. Tumor was found in the re-excision specimen in 42/104 (40%). Local control was significantly reduced in patients with positive margins after definite resection ($p < 0.001$), and in patients with microscopic disease in re-excision specimens ($p = 0.05$). The

frequency of margin positivity in re-excision specimens was not described.⁶² Unplanned excision should be avoided whenever possible.

Recurrence following resection

Local recurrence following previous resection has been associated with an increased risk of local failure following definitive re-excision with or without postoperative radiation. The reasons for this observation are poorly understood. An underestimation of the geographic extent (geographic miss) is not likely given that most recurrences of this nature are in field.²⁸ Underestimation of the extent of tumor at the second excision is possible if the planes of the previous resection are not completely appreciated. A plausible notion is that local recurrence following resection results in selection of biologic (invasiveness) and tumor environmental (hypoxia) factors which make local control less likely.

Dinges *et al.* at the University of Essen, Germany, obtained local control in 94% and 91% of T1 and T2 primary tumors, compared to 55% and 61% for T1 and T2 recurrent tumors ($p = 0.0002$), respectively, following surgery and postoperative radiation. Multivariate analysis identified recurrent tumor at presentation as an independent predictor of local failure. This was so despite the fact that tumors in the recurrent group were significantly smaller (4.5 cm versus 8.0 cm).²⁸ Previous local recurrence was also identified by Singer *et al.* to confer a higher subsequent local failure rate (47%) than nonrecurrent tumors (11%) following definitive resection with or without radiation ($p = 0.0001$).⁴⁰ Reports from MD Anderson by Zagars *et al.*^{43,44} and Pollak *et al.*³¹ also identified locally recurrent tumor at presentation as an adverse predictor of local control in multivariate analyses (local control was only 58–65% at 5 years for tumors presenting as recurrent). Similar findings were reported for surgically treated patients by investigators from Memorial Sloan Kettering Cancer Center.^{33–35}

However, prior local failure has not always been shown to predict local recurrence when adjuvant radiotherapy is employed. There was no difference in local control for primary or locally recurrent tumors following radiotherapy in the series from Amsterdam reported by Keus *et al.*²⁹ Similar rates of local control for primary (75%) and locally recurrent tumors (78%) were obtained at the Princess Margaret Hospital following radiotherapy despite a higher rate of distant failure 42% versus 30%, and worse cause-specific survival for recurrent tumors.³⁷ Although there are no randomized trials which clearly demonstrate improved local control for locally recurrent tumors receiving postoperative radiotherapy, single-institution retrospective series

suggest that the use of postoperative radiotherapy can produce local control rates similar to those obtained following treatment of primary tumors. Therefore, locally recurrent tumor is an indication for postoperative radiotherapy following re-excision.

Volume

The radiotherapy treatment volume remains an area of continued interest and controversy. Initial experience in the postoperative treatment of sarcoma led to the prescription of fields which often extended from origin to insertion of the affected muscle group.¹⁶ Over time, improvements in resection techniques and medical imaging have allowed the radiotherapy treatment volume to be progressively reduced in size. As discussed below, excellent local control of high-grade sarcoma has been obtained with brachytherapy treatment of the tumor bed alone.^{50,63}

Following postoperative external beam radiation, Pao and Pilepich noted 44% local failure with limited radiation volumes (<5 cm), compared to 10% with subcompartmental volumes, and to 19% when the entire compartment was treated. They recommended longitudinal treatment volumes of at least 5 cm.⁴⁷ Mundt *et al.* described local control in only 30.4% of patients treated with postoperative external-beam volumes < 5 cm, compared to 93.2% local control for field margins ≥ 5 cm. No additional benefit was observed for target volumes with margins which exceeded 10 cm.⁶ In the absence of data from a randomized trial demonstrating the equivalent outcome for target volumes less than and greater than 5 cm, volumes ≥ 5 cm should be used in the adjuvant radiotherapy of soft-tissue sarcomas. There is no *proven* indication for target volume reductions in the treatment of low-grade sarcomas.

Dose

Soft-tissue sarcomas can be controlled with moderately high doses of radiation (60–63 Gy) when administered in the postoperative setting.⁶⁴ Retrospective evidence of a dose–response relationship for local control has been reported.^{28,30} Dignes found that, for dose ranges of <50 Gy, 50–60 Gy and >65 Gy, local failure occurred in 31%, 16% and 0%, respectively. Multivariate analysis identified total radiation dose as an independent predictor of local control. However, patients in the lowest dose ranges may have had other risk factors for recurrence (i.e. previous radiation, intra-abdominal or retroperitoneal sites, poor overall condition, etc.).²⁸

Sixty-seven patients treated at Fox Chase/University of Pennsylvania received limb-sparing surgery and postoperative radiation for soft-tissue sarcomas. Overall, actuarial local control at 5 years was 87%. For

patients who received ≤ 62.5 Gy, 82% were locally controlled compared to 97% of patients who received ≥ 62.5 Gy despite there being larger tumors and a higher percentage of high-grade lesions in the group receiving ≥ 62.5 Gy. Multivariate analysis confirmed total dose > 62.5 Gy as an independent predictor of local control.³⁰ In a retrospective study from the University of Miami, investigators reported an increase in survival associated with increasing radiation dose, although local control was not analyzed separately.⁶⁵ The available data suggest that total doses less than 63 Gy may compromise local control when radiation is given postoperatively for soft-tissue sarcomas.

In summary, the literature supports the importance of margin status, tumor location, and previous recurrence as predictors of local control following resection and postoperative radiotherapy. Prognostic factors and their relative predictive values are summarized in Table 5.8.

Preoperative Radiotherapy for Soft-tissue Sarcoma

The optimal sequencing of surgery and radiation in the local treatment of soft-tissue sarcomas has not been resolved. Although the majority of patients treated outside of specialized centers such as Massachusetts General Hospital or UCLA receive postoperative radiation, preoperative radiation has been shown to be a very effective adjuvant to surgery,^{22,66–68} and has certain advantages which are detailed in Table 5.9.

Early experiences with preoperative radiation were reported by McNeer *et al.*¹⁹ From 1935 to 1959 a total of 46 patients received preoperative radiotherapy at Memorial Sloan Kettering. Preoperative radiation was used to shrink bulky tumors in order to facilitate their resection, while surgery only was used for smaller, more favorable tumors which could be resected with wide margin. Postoperative radiation was used if the margins of resection were positive. McNeer *et al.*'s local

control for liposarcoma was 75% following preoperative radiation and resection, and 79% following surgery alone. In contrast, local control following postoperative radiotherapy for liposarcoma was only 57%.¹⁹

Preoperative radiation and concurrent infusional chemotherapy was investigated at UCLA by Eilber and colleagues.^{66,69–72} In their initial experience, 14 patients were treated with intra-arterial infusion of Adriamycin (20–30 mg) every 24 h for 3 days, followed by 350 cGy per day for 10 days for a total of 3500 cGy. One week following completion of radiotherapy, en-bloc resection was performed. Tumor necrosis was seen in 88%, of resected specimens given intra-arterial chemotherapy and radiation, versus 63% following intra-arterial chemotherapy alone. Thirteen of 14 patients had sufficient shrinkage of tumor following preoperative radiation to allow resection. All 13 were locally controlled (local control 93%). This was in contrast to the 50% local control following surgery alone in the same report.⁷⁰ Eilber *et al.* updated the UCLA experience in 1984 having treated 100 soft-tissue sarcomas and 83 bone sarcomas. They reported local control rates of 97% in both groups. The observed complications included arterial thrombus (two patients), wound slough (13 patients), pathologic fractures (five patients), lymphedema (four patients), fibrosis and pyarthrosis (one patient each). Fifty-six percent of bone allografts required revision, and complications of the endoprosthesis occurred in 9%. The overall complication rate in 77 patients with high-grade sarcoma was approximately 30%.⁶⁶ A second UCLA trial addressed the high rate of complication by reducing the total radiation dose to 1750 (five fractions of 350 Gy each). This resulted in an overall reduction of complications to 25%, and a doubling of the local failure rate (i.e. 20%). The third trial randomized patients to intravenous or intra-arterial Adriamycin, with preoperative radiation to 2800 Gy in eight fractions. Local failure decreased to 14% and there was no difference in control or overall

Table 5.9 Pros and cons of preoperative radiation

	<i>Preoperative radiation</i>	<i>Postoperative radiation</i>
Advantage	May improve resectability Radiated target volume is smaller Improves local control for larger tumors Extent of resection may be reduced Decreased risk of tumor implantation	Fewer wound complications Immediate removal of tumor Histologic analysis is facilitated Precise assessment of tumor extent
Disadvantage	Increased postoperative complications Diagnosis is based on limited biopsy material Surgery is delayed during radiation Tumor extent may be difficult to assess	Radiated target volume is larger Radiation is delayed Amputation may be more frequent

survival rate between intravenous and intra-arterial chemotherapy. The next two trials evaluated intravenous Adriamycin plus cisplatin (trial 4) and intravenous high-dose ifosfamide for two cycles followed by Adriamycin and cisplatin (trial 5). Both of these later two trials utilized 2800 cGy in eight fractions of 350 cGy. Local failure rates for trials 4 and 5 were 12% and 2%, respectively⁷² (see Table 5.10).

In the most recent analysis a total of 150 patients have been treated with intravenous ifosfamide, Adriamycin, and cisplatin followed by 2800 cGy and WLE. There have been only five local failures (5/150) for a local control rate of 145/150 (96%) (F. Eilber, personal communication, June 1999). These updated results are currently under preparation for publication. The UCLA trials are summarized in Table 5.10.

Using very similar techniques, investigators at UC Davis treated 25 patients (17 soft-tissue sarcomas and eight bone sarcomas) with preoperative intra-arterial infusion and radiotherapy. Twelve patients received 35 Gy in 10 fractions and 13 patients received 40 Gy in 20 fractions. There were no local in-field recurrences. Roughly 35% of patients developed wound complications. The limb salvage rate for soft-tissue sarcomas was 88% (15/17), and for bone sarcomas it was 75% (6/8).⁷³ Wanebo *et al.* reported a tricenter trial of intra-arterial Adriamycin and preoperative radiation (30–40 Gy) in 10–25 fractions in 66 patients with extremity sarcomas. There was only 1/66 local recurrence (1.5%). Wound complications occurred in 41%.⁷⁴

The use of preoperative radiation without chemotherapy has been popularized by Suit and co-workers.^{22,75,76} When chemotherapy is not used, patients receive approximately 50 Gy to the intact tumor with 5–10 cm longitudinal margin. Resection is carried out 2–3 weeks post-radiation. If the margins are microscopically or grossly positive a postoperative boost dose of 10–25 Gy is delivered to the site of margin positivity within the tumor bed. In early reports a postoperative boost of 14–16 Gy was routinely employed regardless of margin

status.^{22,75} In a more recent report the 10-year actuarial local control following preoperative radiation was 92% (see Table 5.11).⁷⁶

High rates of local control have been reported by others employing preoperative radiotherapy and resection. Karolinska investigators treated 23 patients with preoperative radiation to 40 Gy (two patients received 64 Gy and 76 Gy, respectively), with only 2/23 local failures, one of which was successfully salvaged (ultimate LC = 22/23).⁶⁸ Barkley *et al.* reported 110 patients who received preoperative radiotherapy and resection at MD Anderson Hospital between 1970 and 1984. Doses ranged from 43 to 60 Gy in 180–200 cGy fractions. Eight patients received neutron irradiation totaling 45–58 cobalt Gray equivalent (CGyE). Local control for the group was 90% (11/110 patients failed locally).⁷⁷

Brant *et al.* at the University of Florida at Gainesville treated 58 adult soft-tissue sarcomas of the extremities and trunk with preoperative radiation in 120–125 cGy per fraction twice daily (49/54 patients) to a total dose of 50–60 Gy (median 50.4 Gy). Ninety percent of lesions were high grade, 78% were >10cm and 84% were extracompartmental. Local control was observed in 53/58 (91%). Local failure was higher following positive margins (33%), and for truncal lesions (17%). Eighty-seven percent retained a functional limb.⁷⁸

Mullen and Zagars reported equivalent results with 49.8 Gy given preoperatively to larger tumors compared to 62 Gy given postoperatively to smaller tumors in patients with synovial sarcoma, suggesting that a preoperative dose of approximately 50 Gy may be a preferable strategy for larger tumors.⁷⁹ In contrast to other reported results, investigators at the University of Minnesota found no local control benefit from preoperative radiation. They reported a significantly higher complication rate associated with preoperative radiation ($p = 0.0014$).⁸⁰

Two studies have evaluated the importance of surgical margins on local control following preoperative

Table 5.10 Summary of UCLA trials of preoperative chemoradiation for soft-tissue sarcoma (from ref. 72)

Trial	No. of patients	Chemotherapy	Fractionation schedule	Total radiation dose (cGy)	Local control
1	77	IA Adria	350 cGy × 10	3500	91%
2	137	IA Adria	350 cGy × 5	1750	80%
3	112	IA Adria	350 cGy × 8	2800	86%
4	46	IV, Adria, Plat	350 cGy × 8	2800	88%
5	63	IV, Adria, Plat, IFOS	350 cGy × 8	2800	98%

IA = intra-arterial; IV = intravenous; Adria = Adriamycin – (30 mg/day × 3 days); IFOS – ifosfamide – (2 g/m² × 8 days); Plat = cisplatin – (120 mg/m²).

Table 5.11 Results of preoperative radiation from Massachusetts General Hospital (from ref. 76)

Tumor size	No. of patients	Local control
2.5 cm	11	80%
2.6–4.9 cm	16	100%
5.0–10.0 cm	63	93%
10.1–15 cm	34	100%
15.1–20 cm	25	79%
>20cm	11	100%
Total	160	92%

radiation. Sadoski *et al.* analyzed 132 patients from Massachusetts General Hospital who were treated with preoperative radiotherapy. Local control was achieved in 94%. Local control with negative margins was 97%, while it was only 82% for margin-positive patients ($p = 0.02$). The size of the surgical margin following preoperative radiation had no significant influence on local control (94% for margins ≤ 1 mm, 97% for margins >1 mm, and 100% local control for no tumor in the specimen). Other factors affecting local control in margin-positive patients were: tumor location (upper versus lower extremity) and tumor grade. The authors concluded that little is gained by achieving widely negative margins following preoperative radiation.⁸¹

Tanabe *et al.* reviewed 95 patients who received preoperative radiation at MD Anderson Hospital. Twenty-four of 95 (26%) patients had microscopically positive margins. Local control in margin-negative patients was 91%, while it was 62% when the margins were positive ($p = 0.005$). A Cox model of factors prognostic for local recurrence identified intraoperative tumor violation and positive margins as predictors of local failure.⁸²

An advantage of preoperative radiation is the potential reduction in irradiated volume. This is because the surgically manipulated or operatively exposed tissues must be included in the postoperative radiation target volume. Theoretically, the less extensive (smaller) volumes utilized with preoperative irradiation should reduce chronic radiation-related morbidity. This was evaluated by Nielsen and colleagues, who demonstrated that the radiation field size and the number of joints radiated were significantly less with preoperative, compared to postoperative radiotherapy ($p = <0.001$).⁸³

The major practical disadvantage of preoperative compared to postoperative radiation is its impact on perioperative wound morbidity. Bujko and colleagues reported delays in wound healing in 37% of patients following preoperative radiation. Sixteen percent of

patients required a second surgical revision for treatment of wound complications and 3% required amputation. Factors predictive of wound complications in multivariate analysis included lower versus upper extremity location, estimated blood loss >1 liter, increasing patient age, and bid fractionation.⁸⁴

A randomized Canadian trial of preoperative versus postoperative radiotherapy for soft-tissue sarcoma accrued patients from 1994 to 1997. The study was closed to accrual when preliminary analysis revealed a significantly increased number of wound complications in the preoperative group (35%) compared to the postoperative group (17%). This trial, which has been reported in abstract form only, has so far revealed no difference in local control or disease-free survival for preoperative versus postoperative radiotherapy.⁸⁵

Complication rates for preoperative radiotherapy reported by various authors range from 10% to 41%^{68,72,74,78,80,82,85} The risk of perioperative wound complications is increased with preoperative radiation, despite the smaller target volumes which are radiated. However, a comparison of radiation-induced late effects (i.e. fibrosis, edema and joint dysfunction) among preoperative and postoperative patients has not yet been reported. Despite an increase in wound complications, preoperative radiation appears to improve resectability of bulky tumors,^{19,76} improve local control for tumors >15 cm,⁷⁶ reduce the extent of surgery required to achieve adequate negative margins,⁸¹ and reduce the volume of normal tissue which requires radiotherapy.⁸³

Brachytherapy

Brachytherapy (*brachus*, the Greek root meaning short) is the use of radioactive sources placed close to, or implanted within, the tumor. Radiation implants, or brachytherapy, can be temporary or permanent. Brachytherapy for soft-tissue sarcomas has been used in conjunction with surgery alone, or with surgery and external beam irradiation.^{49,86–88} The most frequently used technique for the treatment of soft-tissue sarcoma employs plastic catheters which are temporarily implanted into the tumor bed at the time of wide local excision (WLE). After closure of the wound, the radioactive 192-iridium or high-activity 125-iodine sources are "after loaded" into the catheters and left in place until the prescribed dose of radiation has been delivered to the tumor bed. Of the several brachytherapy advantages, perhaps the most important is the ability to deliver high doses to the tumor bed while sparing normal tissue 2–3 cm away. Other advantages include: (a) the potential to eliminate the need for 6–7 weeks of outpatient radiotherapy, resulting in a shorter

overall treatment time; (b) treatment is initiated early in the postoperative period, reducing the probability of tumor proliferation, or development of chronic hypoxia which could increase the risk of local recurrence; (c) previously irradiated sites can be safely retreated as a result of the steep dose gradient which allows sparing of nearby normal tissue.

Through a series of clinical studies over the past 25 years, investigators at Memorial Sloan Kettering have documented the development of several technical refinements in brachytherapy for soft-tissue sarcomas, and have established brachytherapy as an attractive alternative to external-beam radiation in adjuvant treatment of high-grade soft-tissue sarcomas. Shiu *et al.* reported an early experience at Memorial with brachytherapy and function-sparing resection for extremity sarcomas. Thirty-three patients were reported, 16 of whom presented with recurrent tumor following previous resection. The median dose delivered via brachytherapy equaled 4000 cGy over 4–5 days. Five patients also received 2000–4000 cGy of supplementary external-beam irradiation over 2–3 weeks postoperatively, and six patients received adjuvant chemotherapy. Local control was achieved in 100% of patients with no prior recurrence and in 10/16 (62.5%) patients with prior recurrences (overall local failure rate = 18%). Thirty-nine percent (13/33) of patients required amputation as a result of treatment complications. Factors related to complications appeared to be high brachytherapy dose (> 5000 Gy) in patients who had received prior radiotherapy (as occurred in the two patients requiring amputation) and suboptimal surgical technique (i.e. poorly vascularized flaps; closure under tension).⁸⁹

An early comprehensive analysis of brachytherapy-related morbidity revealed a significantly increased rate of major and moderate wound complications following brachytherapy (44%) compared to resection alone (14%).⁹⁰ This observation led to several changes in surgical policy,⁹¹ including the use of thick, vascularized flaps, or myocutaneous flaps, and soft-tissue rotation. In addition, radiation sources were after-loaded on the 5th postoperative day to prevent radiation-induced inhibition of wound healing, and attempts were made to limit the radiation dose to healing skin. In a subsequent analysis after implementation of these changes, Ormsby *et al.* reported a significant reduction in wound complications from brachytherapy (down to 14%) when radioactive sources were loaded after the 5th postoperative day, indicating that the timing of source loading is a major factor in brachytherapy-induced wound complications, and that radiation-induced delays in wound closure could be averted by allowing an initial period of wound healing.⁹² These

refinements in brachytherapy technique are outlined in Table 5.12.

While postoperative treatment of sarcomas with brachytherapy alone has been emphasized at Memorial Sloan Kettering, other institutions have utilized brachytherapy as a local boost given in combination with external-beam irradiation. Twenty-five patients with soft-tissue sarcomas were treated with WLE and brachytherapy (nine patients) or WLE, brachytherapy and external-beam radiotherapy (16 patients), at the University of Kansas. Local failure occurred in 5/25 (20%). The only variable identified in a multivariate analysis to predict an increased risk of local recurrence was the ratio of target volume receiving 6500 cGy divided by the tumor volume (TV65/TV). Local recurrence was increased when this volume was less than one. Also of note was that five of seven patients with positive margins experienced local failure.⁸⁶ As found in the Memorial randomized trial (see below), the use of brachytherapy did not by itself mitigate the increased risk of local failure associated with positive surgical margins.^{50,86,93}

O'Connor *et al.*⁹⁴ updated the Mayo Clinic experience with brachytherapy for sarcoma originally reported by Schray *et al.* in 1990.⁸⁷ Sixty-nine patients were reviewed, of whom 68 were evaluated with follow-up. The overall local recurrence rate was 9%. Local failures were numerically more frequent in high-grade tumors (14%), marginal resection (17%) and in tumors with previous local recurrence (29%). Wound complications were more frequent when preoperative radiation was combined with resection and brachytherapy (24%) compared to resection, brachytherapy and postoperative external-beam radiation (15%). Overall local control rates (91%) and wound complication rates (17%) were comparable to resection and brachytherapy alone.⁹⁴

Table 5.12 Refinements in surgical and brachytherapy technique developed at Memorial Sloan Kettering 1975–1996

Surgery

1. Meticulous tension-free closure of skin flaps
2. Use of thick vascularized flaps for closure of soft-tissue defects
3. Use of rotational flaps for closure of soft-tissue defects

Brachytherapy

1. Delay loading of radioactivity until the 6th postoperative day
2. Monitor dosimetry and limit dose to skin to less than 2000 cGy
3. High activity ¹²⁵I seeds with less energetic photon (lower radiation exposure of normal tissues and health-care workers)
4. High dose rate after loading
5. Three-dimensional brachytherapy treatment planning

The only randomized trial of brachytherapy in the treatment of soft-tissue sarcomas was conducted at Memorial Sloan Kettering from 1982 to 1987. Long-term results of this study were reported by Pisters *et al.*⁴⁸ and Harrison *et al.*⁴⁹ One hundred and sixty-four patients with soft-tissue sarcomas were randomized after stratification by age, histology, size, depth, location, margin, and status of the primary, to brachytherapy (78 patients) or surgery alone (86 patients). Randomization occurred in the operating room after a grossly complete limb-sparing resection. Patients typically received a median dose of 4500 cGy prescribed to a point in tissue 0.5 cm away from the target volume which consisted of tumor bed, plus 2 cm longitudinally and 1.5–2.0 cm mediolaterally. Local control was obtained in 83% (13/78 local failures) of those treated with brachytherapy, and in 71% (25/86, local failures) of those treated with surgery alone ($p < 0.04$). Actuarial freedom from local recurrence at 5 years equaled 82% for brachytherapy versus 69% for surgery alone ($p = 0.04$). When analysis was stratified by grade, an improvement in local control was not observed for low-grade tumors. However, there was a substantial improvement in local control for high-grade tumors treated with brachytherapy (89%) versus surgery alone (66%) ($p = 0.0025$). This is shown in Figure 5.3. Age >60 years was an important predictor of local recurrence for the entire group. Multivariate analysis limited to the high-grade group identified age >60 years and absence of brachytherapy as the only significant predictors of local failure. Among those patients with positive margins, local recurrences were *not* significantly reduced by brachytherapy. The use of brachytherapy had no significant influence on disease-specific survival or the risk of distant metastases.^{48,49}

Involvement of neurovascular structures need not be a contraindication to brachytherapy. Forty-five patients reported by Zelefsky *et al.* had en-bloc resection of tumor off of neurovascular structures. Margins were grossly positive, microscopically positive, or <1 mm in (69%). Twenty-eight percent of patients had pathologic evidence of invasion into neurovascular structures. After-loading catheters were placed directly on neurovascular structures and a median dose of 4400 cGy delivered to the target volume. Post-implantation external-beam radiotherapy was given in 13/45 (28%). Local failure developed in 14/45 (31%). Poor implant geometry, and the non-use of post-implant external-beam radiotherapy in the setting of multiply positive margins were associated with local recurrence. Seven patients required amputation of local recurrence. Four patients (8.5%) who received a cumulative dose >90 Gy to the neurovascular bundle developed peripheral neuropathy. Thus a cumulative dose to neurovascular structures of < 90 Gy appeared to be well tolerated.⁹⁵

Alekhteyar and colleagues at Memorial Sloan Kettering analyzed the impact of external-beam radiation in patients with positive margins treated with resection and brachytherapy. One hundred and five patients were reviewed, 87 received resection and

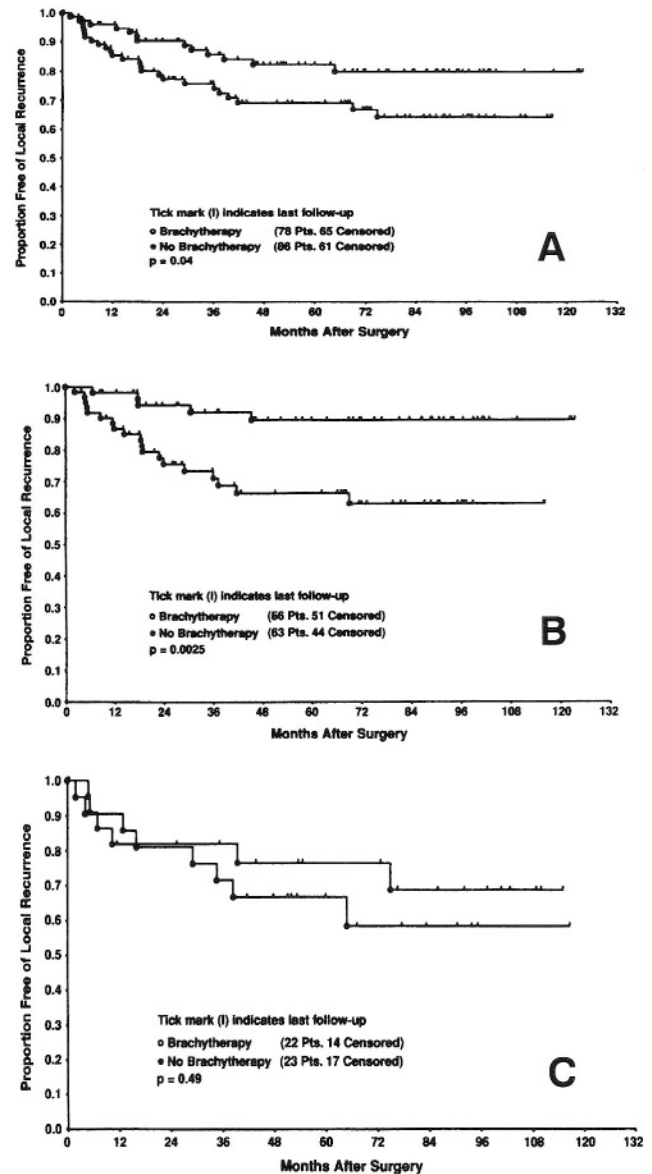


Figure 5.3 Results of the randomized trial of adjuvant brachytherapy for soft-tissue sarcoma at Memorial Sloan Kettering. Actuarial projections of freedom from local recurrence are shown for: (A) the entire study group; (B) 119 patients with high-grade sarcoma; and (C) 45 patients with low-grade sarcoma. There was no significant difference in freedom from local recurrence for low-grade sarcomas treated with brachytherapy. No differences were seen in distant metastasis-free survival or disease-specific survival for those patients treated with adjuvant brachytherapy (from ref. 48).

brachytherapy (45 Gy) and 18 patients received resection, brachytherapy boost (15–20 Gy) and postoperative external-beam radiation (45–50 Gy). The local control rate for the series was 86%. Local control for the brachytherapy-alone group was 82%, and for the brachytherapy radiation and external beam group it was 90% (p not significant). For patients with positive margins, local control following brachytherapy and external beam was 90% compared to 59% for brachytherapy, alone ($p = 0.08$). Multivariate analysis revealed primary tumor (nonrecurrent), and negative margins as predictive of local control. Of note were the similar rates of local control in the compared groups, despite the presence of significantly more tumors with positive margins in the brachytherapy plus external beam group (56%) compared to the brachytherapy-alone group (20%, $p = 0.003$). The authors concluded that the addition of external beam is their current policy for patients with positive margins.⁹⁶

In summary, brachytherapy has a proven role in the treatment of soft-tissue sarcomas following WLE. It is also effective as a boost (15–20 Gy) in combination with external-beam radiotherapy (45–50 Gy). Positive margins following limb-sparing resection appear to be best managed with combined brachytherapy and external beam.^{96,97} Preoperative radiation appears to increase wound complications following resection and brachytherapy.^{87,94} Technical advances in brachytherapy including high dose rate after loading,⁹⁸ high activity ¹²⁵I,^{99,100} three-dimensional treatment planning⁹⁹ and intraoperative magnetic resonance guidance are likely to improve the already good results reported in most series.^{50,86,87,89,91,93–95,97–104}

Intraoperative Radiotherapy

Intraoperative radiotherapy (IORT) is the direct intraoperative application of orthovoltage X-rays or electrons to the exposed tumor, or its bed. The advantage of IORT is the ability to deliver an intraoperative boost to the surgically defined regions of interest (i.e. limited margins, gross residual tumor, etc.) while sensitive normal tissues (bowel, skin flaps, nerves, etc.) are temporarily displaced out of the irradiated field. Early forms of IORT were reported in the first decade of this century,¹⁰⁵ and modern IORT was developed in Japan in the 1960s and then in America at Howard University in the 1970s. IORT has been used more frequently for retroperitoneal sarcomas than for sarcomas arising in extremities or other locations. The results of IORT for retroperitoneal sarcomas will be discussed with other treatments for retroperitoneal sarcomas.

Twenty-five patients with extremity soft-tissue sarcomas received IORT at the University of Heidelberg

between 1991 and 1995. A mean dose of 15 Gy was delivered intraoperatively via a dedicated linear accelerator in the operating suite capable of producing electron beam energies from 6 to 18 MeV, corresponding to the ability to penetrate tissue to depths ranging from 20 to 54 mm. All patients also received external-beam irradiation 3–6 weeks after the operation to a mean dose of 44 Gy. Local control was achieved in 92% of patients with a median follow-up of 26.8 months. One out of four patients (25%) with positive margins had local failure compared to only one out of 21 (4%) with negative margins. Three patients had wound healing complications and six patients developed severe late complications, including: pathologic fracture in two patients; limb contracture in two patients; and tibial osteitis and neuropathy in one patient each. Overall and disease-free survival levels were lower for high-grade lesions, consistent with an increased risk of metastatic relapse in that group.¹⁰⁵

Haddock *et al.* reported 91 patients treated with IORT for extremity and limb girdle sarcomas at the Mayo Clinic from 1986 to 1995. Sixty-three patients had high-grade lesions and 28 had low-grade lesions. Tumors were located in the upper extremity in 20 patients, lower extremity in 54 patients and limb girdle in 17 patients. Seventy-four patients had primary tumors and 17 had recurrent tumors. IORT doses ranged from 7.5 to 20 Gy (median 10 Gy). Eighty-eight patients also received external-beam radiotherapy (69 received preoperative and 19 received postoperative irradiation) to a median dose of 50.4 Gy. Thirty-nine patients had microscopically positive margins (43%), 38 had close margins (42%), one patient had gross residual disease. Margins were negative in 13 patients. Local control with a median follow-up of 3 years was 92%. There were 6/91 local failures, one of which was within the IORT boost field. Overall survival at 3 years was 76%. Data describing the frequency of failure as a function of resection margin were not disclosed.¹⁰⁶ However, these results are quite favorable given that 39/91 patients (43%) had positive margins. Longer follow-up is needed to confirm these excellent results.

High LET and Proton Therapy

Alternative forms of radiation have been utilized in the treatment of soft-tissue sarcomas. High linear energy transfer (LET) radiation refers to those forms of radiation which produce more dense energy transfer (ionization) per unit path length in tissue. Examples of high-LET radiation include alpha particles, neutrons, neon and argon ions. The radiobiologic advantages of high-LET radiation include: (a) reduced oxygen dependence; (b) a higher yield of DNA double-strand

breaks; and (c) cell killing which is less dependent on cell cycle distribution. LET for various forms of radiation is shown diagrammatically in Figure 5.4.

Early neutron therapy trials produced higher local control rates than those achieved with X-rays; however, toxicities were also higher. Catterall treated 28 patients with 16 MeV neutrons to a total dose of 1560 neutron rads over 4 weeks. Twenty-one of 28 (75%) patients were locally controlled, yet 9/28 (32%) developed major complications.¹⁰⁷ The high complication rate was likely a result of the inadequate depth dose characteristics of the 16 MeV neutron beam. Higher beam energies deliver their maximum dose deeper in tissue, allowing relative sparing of skin and subcutaneous tissues.

Investigators at MD Anderson Hospital treated 34 patients with locally advanced, unresected sarcomas at the Texas A&M Variable Energy Cyclotron (TAMVEC). In the early years of this pilot study, patients were treated with 16 MeV neutrons, and after 1972 a higher-energy 50 MeV neutron beam was used. The higher-energy neutron beam produced a depth of maximum dose (D_{max}) of 8 mm, and at 10 cm delivered 63% of the D_{max} dose, compared to a D_{max} of 2 mm, and 41.3% of D_{max} at 10 cm with the 16 MeV beam. Local control for the 29 patients with soft-tissue sarcomas was 69%. A variety of fractionation schemes and combinations with X-ray therapy were used. Only one of four patients with chondrosarcoma was controlled and the one patient with osteosarcoma had persistent local disease following irradiation. Four patients (4/34, 11%) developed a major complication; two of these were skin ulcerations following treatment with the 16 MeV neutron beam. One patient developed a vesico-vaginal fistula following a 50 MeV neutron boost combined with 25 MeV X-rays to a total dose of 7610 rad equivalents.¹⁰⁸

One hundred and ninety-nine patients with soft-tissue sarcomas were treated with neutron irradiation at the Swiss Institute of Nuclear Research (SIN). Local control for grade I, grade II, and grade III tumors was 76%, 53% and 40%. The corresponding 5-year survival rates were 77%, 63.1% and 34%. Local control was 49% for gross residual disease, 84% for microscopic disease and 95% for completely resected tumor with negative margins. Complication rates decreased from 22% to 15% when neutron irradiation was limited to a boost combined with photons, rather than when it was used for the entire treatment. However, numerically lower rates of local control were also observed following neutron "boost" compared to neutrons alone.^{109,110}

Richard reported on 75 patients with soft-tissue sarcomas treated with neutrons at the Catholic University in Belgium. Forty-seven patients were treated following "radical" resection and 28 patients had large inoperable, incompletely resected or recurrent tumors. Local

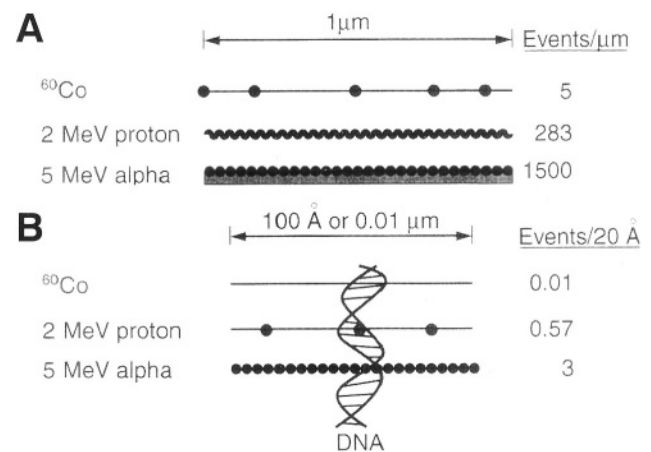


Figure 5.4 The frequency of ionization events along the tracks of various forms of radiation which markedly differ in linear energy transfer (LET). Ionization events over 1 micron (1 μm) are shown in (A), and events over a distance of 100 angstrom (100 Å) are shown in (B). The dimensions of a DNA molecule are represented by the double helix (redrawn from Tannock IF, Hill RP, editors. *The Basis of Science of Oncology*, 3rd edn. New York: McGraw Hill; 1998).

control rates for each group were 43/47 (92%) and 5/28 (18%), respectively.¹¹¹

Pickering *et al.* described the Hammersmith Hospital in London experience with neutrons for soft-tissue sarcomas. Sixty-six patients were retrospectively reviewed who had received 1560 neutron cGy in 12 fractions over 28 days. Fifty of the 66 patients (75%) had palpable tumor, and 31 patients had tumors >10 cm, of which more than 50% were grade 3 lesions. Local control in the 16 patients with negative margins was 94% (15/16), and the 5-year survival for this group was 86%. Complete regression was noted in 34/50 (68%) of patients with palpable gross disease. The overall local control rate for palpable tumors was 52%. Forty-one percent of patients developed late complications, mostly involving skin as a result of the poor depth of penetration of the low-energy neutron beam.¹¹² In a review of the world literature for fast neutron therapy for soft-tissue sarcomas, Griffin *et al.* reported a local control of 50% for patients with gross or unresectable disease.¹¹³ These results appear superior to those reported for photon radiation alone.^{15,16,20,25}

Pi-mesons (pions) are high-LET particles that share the biologic advantages of neutrons, yet also possess the dose distribution advantages of charged particles. The Bragg peak phenomenon, characteristic of pions, protons and other charged particle radiation, is shown diagrammatically in Figure 5.5. The large deposition of ionizing energy at a discrete depth resulting from the Bragg peak produces radiation dose distributions

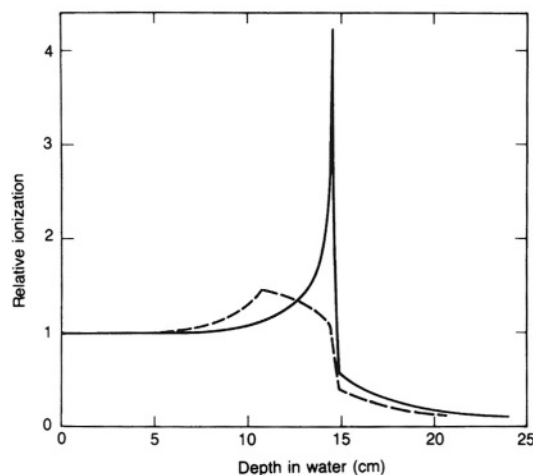


Figure 5.5 The Bragg peak is the sudden, large deposition of energy which occurs at a depth in tissue where the kinetic energy of a charged particle has been sufficiently depleted to allow a close interaction with an oppositely charged particle (i.e. an electron or proton in tissue). The characteristically sharp Bragg peak is compared to a modulated Bragg peak used for clinical treatment. Despite the spreading out of the modulated peak, a sharp decline in dose beyond a certain depth remains (redrawn from Perez C, Brady L, editors. *Principles and Practice of Radiation Oncology*. Philadelphia: Lippincott; 1992).

which are superior to those produced by X-rays. A comparison of depth dose characteristics of various heavy particle beams is shown in Figure 5.6. In addition to the advantage of Bragg peak dosimetry, pions possess higher LET than X-rays which results in more effective cell killing. Greiner *et al.* reported the Paul Sherrer (formerly SIN) Institute experience with unresectable sarcomas treated with pion radiotherapy. Thirty-five patients were treated; three following gross excision of tumor, nine following partial resections, and 15 following biopsy only. Eight patients were treated with low-dose therapy (7–27 Gy) and 27 patients received high-dose (30–36 Gy) therapy. Local control for the 27 patients in the high-dose group was 64%. Late reactions occurred in 28% of patients, and they were severe (grade III or IV) in 18%. One patient each developed skin necrosis, impaired erection, liver toxicity, leg edema and small bowel obstruction.¹¹⁴ This experience compares favorably to results with conventional photon therapy alone for gross disease.^{15,16,20,25}

Protons also produce Bragg peak dosimetry in tissue. The depth dose characteristics of a clinical proton beam are shown diagrammatically in Figure 5.7. Protons have biological effects which are similar to photons or X-rays; however, the dosimetry of protons resulting from the Bragg peak allows higher doses of radiation to be delivered to regions closer to critical structures. Protons have been used in the treatment of soft-tissue sarcomas

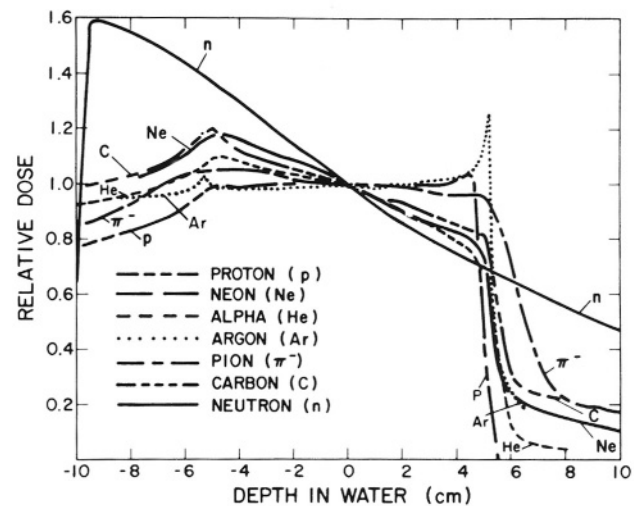


Figure 5.6 The depth dose characteristics of several heavy particle beams with modulated Bragg peaks are compared to neutrons (n) which have depth dose characteristics similar to low-energy photons (X-rays) (redrawn from Kahn F, *The Physics of Radiation Therapy*, 2nd edn. Baltimore: Williams & Wilkins; 1994).

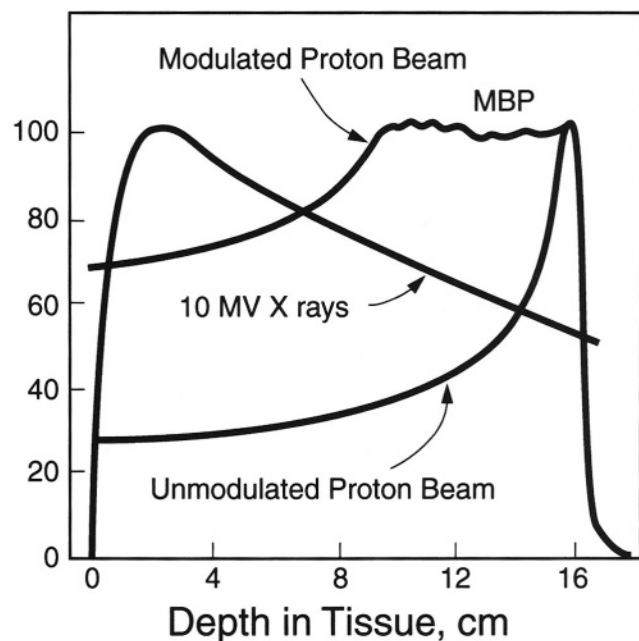


Figure 5.7 Modulated Bragg peak which is utilized for clinical proton therapy. Note that while the peak of the radiation dose is spread out as a result of beam modulation, the fall-off of dose at depth remains very sharp. That is what makes charged particles so useful in treating tumors which lie very close to dose-limiting critical structures. The modulated Bragg peak (MBP) is produced to allow a homogeneous dose to be delivered within a tumor of a given thickness at a given depth in tissue. Proton beam modulators typically consist of paraffin "tissue-equivalent" material of varying thickness, which are placed in between the beam source and the patient (redrawn from Liebel S, Phillips T, editors. *Textbook of Radiation Oncology*. Philadelphia: Saunders; 1998).

at Massachusetts General Hospital with local control achieved in 86%.¹¹⁵ However, proton therapy has perhaps been most useful in the treatment of osteogenic or chondrogenic tumors of the skull base or axial skeleton. Hug *et al.* reported 47 patients with bone sarcoma who were treated at the Massachusetts General Hospital Harvard Cyclotron Facility with proton therapy. In this series, patients were grouped as follows: group 1 (14 chordoma and six chondrosarcoma); group 2 (15 osteogenic sarcoma); group 3 (eight giant-cell tumors, two osteoblastoma and two chondrosarcoma). Patients received proton radiation alone, or photon therapy with a proton boost (preoperatively and/or postoperatively). Seven patients were treated following biopsy only. Local control for group 1 was: 9/14 (64%) for chordomas and 6/6 (100%) chondrosarcomas. Local control for group 2 was 11/15 (73%) and local control in group 3 was 10/12 (83%). Late toxicities were similar to those experienced following conventional radiotherapy.¹¹⁶

In summary, charged particle and high-LET therapies offer promise in the treatment of unresectable soft-tissue and bone sarcomas. Improvement in beam technology will allow higher energy, more deeply penetrating beams to be produced at a lower cost with greater convenience. With optimization of dose distributions through the use of three-dimensional treatment planning and better depth dose characteristics, the results for locally advanced unresectable tumors should continue to improve.

Radiosensitizers

Many chemical agents have been shown to modify the cellular responses to radiation.^{117–119} Early recognition of the importance of tumor hypoxia led to the development of agents which sensitize hypoxic cells. Hypoxic cell sensitizers were extensively tested in the 1970s and 1980s without significant improvements in local control when combined with radiation. Misonidazole, an *in-vitro* hypoxic cell sensitizer, was administered to 10 patients with sarcomas (seven osteogenic sarcoma, one low-grade, one undifferentiated and one chondrosarcoma) treated at the National Cancer Institute (NCI). Radiation was administered in 400–450 cGy fractions to a total of 40–50 Gy. There were no complete responses. Seven out of 10 (70%) patients experienced no further growth of the primary tumor during follow-up. Autopsy in one patient revealed persistent osteoid matrix and no viable tumor cell.¹²⁰

Halogenated pyrimidines constitute a different class of radiosensitizers. These agents are incorporated into the DNA of actively cycling cells, resulting in an increased yield of DNA double-strand breaks following

radiation exposure. Bromodeoxyuridine (BUDR) and iododeoxyuridine (IUDR) have been used in the treatment of soft-tissue sarcomas and osteosarcomas.^{120–122}

Martinez *et al.* reported high local control and high complication rates following treatment of osteosarcoma with BUDR and hypofractionated radiation (see section on osteosarcoma later in this chapter).¹²¹

A series of patients with soft-tissue sarcomas were treated at the NCI with halogenated pyrimidine radiosensitizers. Five patients were initially treated with BUDR and once-daily radiotherapy for unresectable soft-tissue sarcomas. Three out of five (60%) were locally controlled.¹²⁰ A second cohort of 14 patients were treated with IUDR and twice-daily radiation. Twelve of 14 (86%) were locally controlled, with six patients (43%) achieving a complete response and four others (28%) having >50% reduction in tumor size, for an overall response rate of 71%. An update of the NCI experience was reported by Goffman *et al.* Thirty-six patients with large or massive sarcomas were treated with infusional IUDR and twice-daily radiotherapy to 70–75 Gy. All lesions were considered unresectable except in two patients who refused hemipelvectomy. Four patients did not complete radiotherapy, and local control for those who did complete treatment was 62% (20/32).¹²²

Preoperative radiation and infusional IUDR was studied in 37 patients with locally advanced or unresectable sarcomas at the University of Michigan. Four patients developed distant metastases shortly after treatment, and one patient was lost to follow-up. There were no complete responses and five (14%) had a partial response. Twenty-eight patients (28/37, 76%) underwent surgical resection. Thirteen out of 28 (46%) were resected with negative margins and 7/10 patients with previously unresectable extremity sarcomas were resected with negative margins. Late toxicities requiring surgical intervention developed in six patients, and one patient died of cholangitis believed to be secondary to treatment of a retrohepatic sarcoma. Overall, local control was obtained in 75% (27/36). The authors concluded that halogenated pyrimidine sensitizers improved the resectability of advanced limb and truncal sarcomas.¹²³ Comparisons of halogenated pyrimidine radiosensitizers to other preoperative regimens, including radiotherapy alone, warrant further study.

Razoxane (ICRF 159) is an agent which was shown over 20 years ago to hold promise as a radiosensitizer. Laboratory studies demonstrated its ability to radiosensitize tumors through blocking dividing cells at the G2/M phase of the cell cycle (the most radiosensitive phase). A randomized trial of razoxane and radiotherapy versus radiotherapy alone for soft-tissue sarcomas was initiated in 1978. Sixty-six patients were treated with radiation alone and 64 patients received radiation

and razoxane. For those patients treated postoperatively, local control was 81% (21/26) for the razoxane group, and 73% (16/22) following radiation alone. For patients treated with gross disease, local control and complete response rates were 30% and 26% following radiation only, versus 64% ($p = 0.001$) and 38% for the razoxane group. There were no significant differences in survival or late effects between treatment groups.¹²⁴

Despite the variety of molecular targets, and the considerable resources which have been invested in the development of radiosensitizers, none have emerged as significant clinical adjuvants to radiotherapy. However, it is likely that the future will witness further clinical trials with drugs which specifically target signal transduction, growth factor receptors, angiogenesis, proteasome inhibition, transcriptional silencing, apoptosis, cell cycle check points, and DNA repair as mechanisms of radiosensitization. Locally advanced or unresectable soft-tissue sarcomas will remain excellent clinical models to test new strategies for radiosensitization.¹²⁴

Retroperitoneal Sarcomas

Sarcomas of the retroperitoneum represent a unique challenge to surgeons and radiation oncologists. Despite the relative rarity of these tumors, their importance cannot be overemphasized when it is considered that the solutions to the unique problems posed by these tumors have application to other more common malignancies such as colorectal cancer, gynecological cancers and other intra-abdominal or pelvic malignancies. Retroperitoneal sarcomas (RPS) are characterized by: (a) locally advanced disease at presentation; (b) proximity to vital structures; (c) infiltrative growth; (d) frequent peritoneal dissemination; and (e) the limited radiation tolerance of adjacent normal tissues.

Pretreatment prognostic factors which affect disease-free and overall survival include: high grade, the number of mitoses, age, previous recurrence, histologic type, size >10cm, and the presence of metastatic disease.^{125–129} The most important treatment factor influencing local control and survival is the completeness of resection (i.e. status of surgical margins).^{125–128,130–132}

Local recurrence following surgery alone is 34–80%.^{52,125,129,133,134,137} That survival is highly dependent on local control is suggested by the predominance of local failure at the time of recurrence (60% of recurrences are local) and by the presence of local recurrence in 60–100% of patients who die of disease.¹³⁶

Radiation therapy improves local control and may change the pattern of relapse. However, radiotherapy has not been proven to increase survival. It is unlikely that local radiotherapy, in the absence of effective

regional/systemic treatment, will have a major influence on survival. This is due to the propensity of RPS for regional metastases and the proximity of dose-limiting normal structures.

An early experience with radiotherapy for RPS was reported from Memorial Sloan Kettering by Kinne *et al.* Thirty-four patients were treated with complete resection \pm radiation (11 patients, group I), incomplete excision plus \pm radiation (15 patients, group II), and biopsy plus radiation (eight patients, group III). The disease-free interval for the group I patients was 35 months with radiation and 40 months without radiation. For group II the disease-free interval was 32 months with radiation and 16 months without radiation. There were only two long-term survivors in group III; one well-differentiated liposarcoma who was disease-free for 30 years, and one with liposarcoma who presented with local and metastatic recurrence 10 years postirradiation. Nineteen of 34 (56%) patients developed metastatic disease, all of whom also had local recurrence. Although radiotherapy techniques in this series varied considerably through the years, most patients received 50 Gy for definitive treatment of gross disease, and 40 Gy as adjuvant treatment. The clearest benefit of radiotherapy seemed to be in the delay of local recurrence in those patients with partially resected tumor (group II).¹³² In a second report from Memorial Sloan Kettering, by Fortner *et al.*, 27 patients had complete excision of their RPS, 10 of whom received adjuvant radiation. The 5-year disease-free and overall survival rates were 30% and 50% following surgery and radiotherapy versus 12% and 12% following surgery alone.¹³⁷

In the Massachusetts General experience, reported by Tepper *et al.*, the local control and 5-year survival were 54% and 54%, respectively in 17 patients treated with curative intent. Four of six patients who received < 50 Gy developed local recurrence compared to 1/11 patients treated with > 50 Gy.¹³⁸ Harrison *et al.* reviewed 23 patients with RPS referred for radiation therapy at Yale. Out of 23 patients referred, only five had complete or partial resection. Three out of five (60%) were locally controlled at 5 years following radiotherapy. One of these three patients had a recurrence locally at 73 months.¹³¹

Eleven patients with RPS were treated with complete resection followed by 50–64 Gy external-beam radiotherapy at St Bartolo Hospital in Vicenza, Italy. Local control was obtained in 64% (7/11), yet 2/7 (28%) locally controlled patients developed metastatic disease. At 4 years 64% (7/11) patients are alive and 45% (5/11) are alive without disease.¹³⁹ The Netherlands Cancer Institute experience describing 34 patients treated with curative surgery \pm radiation was reported

by Van Doorn *et al.* Four patients had incomplete resection leaving 30 patients with limited (22) or extended (8) surgical margins. Thirteen patients received postoperative radiation. Local recurrence with or without metastatic disease developed in 23/34 patients (68%). Ten patients developed distant metastases, all in association with local recurrence. Six of 13 (46%) who received adjuvant radiotherapy were locally controlled compared to 3/19 (16%) who did not receive radiation ($p < 0.01$).¹⁴⁰

From 1975 to 1988, 104 patients with RPS were seen at the Princess Margaret Hospital in Toronto. All surgery was performed at outlying institutions. Forty-two patients had complete resection (43%), 57 patients (55%) had gross residual disease or biopsy only, and two patients had unknown extents of residual disease. Of the 42 completely resected tumors, 39 (93%) had microscopically positive margins. The median dose of radiotherapy was 40 Gy. The locoregional relapse-free rate was only 28% and 9% at 5 and 10 years, respectively. Overall survival was 36% and 14% at 5 years and 10 years, respectively. The locoregional relapse-free rate for the patients who were completely resected was 55% and 22% at 5 and 10 years, respectively. In the group of patients with complete resection, those who received radiotherapy had a prolonged median time to recurrence (103 months) compared to those who received no radiation (30 months). When the comparison was limited to tumor bed recurrences there was a significant difference between those who received radiation (36 patients) and those who did not (nine patients) ($p = 0.02$).¹⁴¹ The low doses of radiation and the preponderance of positive margins and gross disease in this study bias the results against adjuvant radiotherapy, and therefore support the validity of the improvement in local control associated with radiotherapy.

Fein *et al.* reported the Fox Chase/University of Pennsylvania experience with 21 RPS patients treated from 1965 to 1992. Two patients received preoperative radiation and 19 received postoperative radiation. Brachytherapy or IORT boost was used in 5/21 patients. Radiation doses ranged from 36 to 90 Gy, with a median of 54 Gy. Margins of resection were clearly negative in one patient, close in two patients and either grossly or microscopically positive, or unknown, in the remaining patients. For patients with grossly positive margins the median radiation dose was 59.4 Gy. Follow-up ranged from 14 to 340 months. The actuarial local control at 5 years was 72%. Survival at 2 and 5 years was 69% and 44%, respectively. Local failure occurred in only 2/8 (25%) of patients who received a total dose > 55.2 Gy, compared to 5/13 (38%) of patients who received < 55.2 Gy.¹³⁴ Although these results appear encouraging, follow-up is not mature for all

patients reviewed in this retrospective analysis since locoregional failures can continue to occur for 10 years or longer.¹⁴²

Dynamic three-dimensional conformal pion therapy was used to treat 21 RPS at the Paul Scherrer Institute in Bern, Switzerland. The median target volume treated was approximately 1000 ml and the median pion dose used was 32.3 Gy. Radiation with or without chemotherapy was used in 14 patients, and radiation plus resection was used in seven patients. The median follow-up was 24 months (range 12–75 months). Local control (described as absence of growth and control of symptoms) was obtained in 18/21 (90%) of patients. The actuarial 3- and 5-year local control was 90% and 60%, respectively. The projected 3- and 5-year survivals were 67% and 33%, respectively. Toxicities included mild enteritis during radiotherapy, leg edema, skin fibrosis, impaired hepatic function, and two cases of bowel obstruction felt to be a result of non-radiation-related complications. The limited follow-up and lack of histologic confirmation of tumor response does not allow definitive conclusions regarding the effectiveness of pion therapy for RPS.¹⁴³

The bulk of the evidence appears to support the observation that radiation therapy improves local control in RPS. Indeed, in an analysis of prognostic factors among 48 patients with RPS who survived more than 5 years, radiation therapy was the only factor which significantly predicted a reduced risk of local recurrence.¹²⁶

Intraoperative Radiation Therapy for RPS

In order to avoid the limitations on radiation dose escalation imposed by neighboring organs such as small bowel, novel techniques such as IORT have been used with mixed results in the treatment of RPS.

Willet and colleagues at Massachusetts General Hospital treated 20 RPS patients with preoperative (19 patients) or postoperative (one patient) external-beam radiation (40–50 Gy) and IORT (15 Gy for microscopic disease and 20 Gy for gross residual disease; range 10–20 Gy). Patients received 100% oxygen breathing during IORT. Of the 20 patients treated with this regimen, one patient developed metastatic disease prior to resection and was not explored, and two patients who had diffuse peritoneal sarcomatosis at laparotomy were not resected. Seventeen patients had partial or complete resection, and IORT was used in only 12 patients due to tumor bed sizes which exceeded IORT capabilities in five cases. Three of the five patients not receiving IORT were treated with postoperative radiation. The actuarial local control for the 17 patients resected with or without IORT was 81% at 4 years.

Local control was obtained in 9/12 (75%) among those patients who received IORT. Both patients with gross residual disease treated with IORT failed locally. There were no local failures in the three patients who were treated with preoperative *and* postoperative radiation without IORT. IORT-related toxicities included hydronephrosis accompanied by radiation neuropathy in two patients.¹⁴⁴

Similar results were reported by Gunderson from the Mayo Clinic. Twenty patients (10 primary and 10 recurrent) received resection, IORT and preoperative or postoperative radiotherapy. Twelve were high grade and eight were low grade. Residual disease was microscopic in 11 patients and gross in nine patients. External-beam doses ranged from 45 to 60.4 Gy. IORT doses were 10–12 Gy for microscopic residual disease and 15–20 Gy for gross disease. Follow-up ranged from 9 to 69 months with a minimum of 15 months follow-up on all living patients. Local control within the irradiated sites occurred in 16/20 patients (80%). Regional failure outside of the irradiation fields occurred in two patients (10%). In total, locoregional failure occurred in 6/20 patients (30%). Metastatic failures were more numerous in primary patients (due to the higher percentage of high-grade tumors), and local failure was more frequent with recurrent tumors. The actuarial 5-year survival was 48.5%. Six patients developed significant treatment-related complications: small bowel obstruction following surgery and postoperative radiation in one patient, motor neuropathy in one patient, wound complications in two patients, a urologic complication in one patient, and fibrosis in one patient.¹⁴⁵

A third pilot experience was reported by Bussieres *et al.* from Bordeaux, France. Nineteen patients with RPS received IORT: 14 with primary and five with recurrent tumors. IORT doses ranged from 15 to 20 Gy. Thirteen of 19 patients also received external-beam radiation. The median follow-up was 17 months (range 4–37 months). There were four locoregional recurrences (21%) and three (16%) patients had metastatic disease as their first site of failure. The actuarial local control and survival at 2 years was 76% and 60%, respectively. Observed complications included: lymphedema in two patients, lumbar plexopathy in one patient, chronic enteritis in two cases, and one fatal external iliac artery rupture.¹⁴⁶

The three IORT pilot studies described above, while encouraging, do not clearly support the role of IORT in the treatment of RPS beyond documenting its feasibility and associated toxicities. The results described are not clearly superior to those achieved with postoperative radiation alone, and with small patient numbers and limited follow-up, conclusions are tenuous at best.

Indeed Heslin *et al.* documented a continuing risk of local failure which was approximately 5% per year.¹²⁶

Several of the issues regarding published IORT results were addressed by Sindelar *et al.* in the final results of the NCI prospective randomized trial.¹³⁶ In that study 35 patients without metastatic disease were randomized to resection and postoperative high-dose radiotherapy (20 patients), or resection, IORT and postoperative low-dose radiotherapy (15 patients). All patients received misonidazole 15–30 min prior to IORT. The IORT dose equaled 20 Gy. An actual protocol IORT treatment is shown in Figure 5.8. Postoperative low-dose radiation given to IORT patients equaled 35–40 Gy over 4–5 weeks. High-dose radiotherapy in the control arm consisted of 35–40 Gy followed by a coned-down boost for an additional 15 Gy. All patients were followed with routine examinations every 3–4 months until death. Median follow-up equaled 8 years and the minimum follow-up was 5 years. The median overall survival favored the control group (IORT 45 months; control 52 months), but the difference was not significant. Failures were scored as local (“in-field” recurrences within the abdomen or retroperitoneum region encompassed by the radiotherapy portal), locoregional (within the abdomen or retroperitoneum including diffuse peritoneal sarcomatosis), and distant. There was no significant difference in disease-free survivals between the two groups; however, IORT did have a significant impact on the pattern of disease relapse. While the median time to locoregional recurrence for the IORT group was 63 months compared to 38 months for the control group ($p = 0.4$), the time to in-field local recurrence was significantly longer in the IORT group (127 months), compared to the control group (38 months) ($p < 0.05$). The local failure rate was significantly reduced by IORT. There were 6/15 (40%) local failures with IORT compared to 16/20 (80%) in the control group ($p < 0.05$). IORT patients had a higher rate of metastatic recurrence as the first site of recurrence (50%) compared to the control group (19%). The results of this, the only randomized trial of retroperitoneal sarcomas ever published, are summarized in Table 5.13. Gastrointestinal complications were more frequent in the control group. Chronic enteritis occurred in 12 control patients and in only one IORT patient ($p < 0.01$). Neurologic complications (peripheral neuropathy) developed in nine IORT patients compared to only one control patient ($p < 0.01$). Three IORT patients treated with large IORT treatment portals in the region of femoral and sciatic nerve roots had permanent motor weakness. The authors concluded that IORT improves local control and is associated with lower gastrointestinal toxicity in comparison to conventional radiotherapy. A reduction



Figure 5.8 Intraoperative radiotherapy for a retroperitoneal sarcoma. In (A) the patient, with a lucite electron cone in place over the tumor bed, is being positioned or "docked" below the gantry of the intraoperative accelerator immediately prior to radiation. (B) The patient, "docked" in place, is receiving intraoperative radiation. While the beam is on, all health-care personnel are required to vacate the treatment vault/operating suite, including the anesthesiologist. Closed-circuit television cameras monitor life-support function and several key points including the tumor bed as viewed through the electron cone from the direction of the beam source.

in IORT dose to 15 Gy was recommended, since similar doses had not previously been associated with neuropathy. In this mature study (77% of patients had died), IORT was not significantly superior to conventional radiotherapy in prolonging survival. However, IORT did change the natural history of RPS and was reasonably well tolerated.¹³⁶ With the development of more effective systemic chemotherapy, and further progress in optimizing the clinical radiobiology of IORT to widen the differential between tumor cell kill and normal tissue toxicity, IORT could have a more standard role in the management of RPS. For now

Table 5.13 Results of the NCI randomized trial of IORT for retroperitoneal sarcoma

	<i>IORT</i>	<i>Control</i>	<i>p-Value</i>
<i>Actuarial results</i>			
Overall survival	45 months	52 months	0.39
Disease-free interval	19 months	38 months	0.58
Time to locoregional recurrence	63 months	38 months	0.40
Time to in-field local recurrence	> 127 months	38 months	<0.05
<i>Patterns of recurrence</i>			
<i>First sites</i>			
Local in field	3/10	10/16	0.23
Diffuse locoregional	2/10	2/16	0.63
Distant metastases	5/10	3/16	0.19
<i>Sites at death</i>			
Local in field	3/10	16/16	<0.001
Diffuse locoregional	3/10	6/16	0.99
Distant metastases	5/10	6/16	0.69

IORT remains investigational.

In summary, the most important prognostic predictor of survival in patients with RPS is completeness of resection. Conventional radiotherapy has been shown to improve local control in retrospective series. However, its role has not been proven in a randomized trial. IORT can reduce, but not eliminate, the local failure of RPS. Because the dominant mode of failure and death is intra-abdominal/regional retroperitoneal relapse, development of novel approaches to locoregional therapy will continue to be an important goal in the treatment of RPS.

BONE SARCOMAS

Ewing's Sarcoma

Ewing's sarcoma is a member of a family of poorly differentiated, small, round-cell tumors, the molecular biology of which was recently reviewed.^{147,148} Ewing's sarcoma is responsive to chemotherapy and radiation. Historically, recommendations regarding the management of Ewing's sarcoma initially de-emphasized, and now re-emphasize the role of surgical resection in treatment of the primary site. While there have been no randomized comparisons of surgery and radiation for treatment of the primary site, several retrospective and nonrandomized prospective studies have documented superior local control and superior event-free survival associated with surgical resection.^{149–159} With few exceptions, resection has been utilized for patients who would have a favorable outcome regardless of the form

of local management. Indeed several authors have identified poor prognostic factors more frequently in patients treated primarily with radiation.^{153,156,158,160}

The contemporary treatment of Ewing's sarcoma has as its cornerstone multi-agent chemotherapy containing Adriamycin. Management of the local tumor is individualized. Surgery is favored for expendable bones, and whenever possible as long as organ and limb functional integrity are preserved. In all other circumstances local control with good to excellent functional results can be achieved in 70–100% of cases with induction chemotherapy and optimal radiotherapy techniques.^{161–168} Recognition of the patterns of local failure and the need to reduce the risk of radiation late effects, including second cancers, continue to stimulate efforts to refine radiotherapy doses and volumes.^{155,157}

Radiotherapy has been the dominant treatment of Ewing's sarcoma for most of this century. James Ewing's initial description of "diffuse endotheloma of bone" in 1921 noted the responsiveness of this tumor to radium treatment.¹⁶⁹ This was further demonstrated by C. C. Wang, who reported 50 patients with Ewing's sarcoma treated at the Massachusetts General Hospital from 1930 to 1952. Local control was obtained with radiation alone in 15/22 (68%) patients, and four patients (18%) treated with curative intent survived without disease for 6–13 years.¹ In the University of California San Francisco experience from 1935 to 1970, reported by Phillips and colleagues, 13/16 (72%) of patients were locally controlled with radiation alone, and 24% survived 5 years or longer.² These series, which predate the discovery of effective chemotherapy and the development of limb-sparing surgical procedures, clearly documented the effectiveness of radiation as an alternative to amputation in the 70–80% of patients who would eventually have succumbed to metastatic disease, and documented the curative potential of radiotherapy in approximately 20% of patients without metastases. The practice of irradiating the entire bone, and the use of tumor doses above 5000 rad, resulted from these early experiences.^{1,2,170}

The development of effective chemotherapy regimes in the 1970s ushered in a new era in the treatment of Ewing's sarcoma. This was accompanied by refinements in surgical limb-sparing techniques for bone tumors. Multiagent chemotherapy improved 5-year survival (60% with Adriamycin-containing chemotherapy in the first Intergroup Ewing's Sarcoma Study (IESS-I) compared to 18–24% without chemotherapy), as well as local control.¹⁷¹ As patients began surviving longer, the chronic toxicities of radiation became more apparent and less acceptable. Efforts to improve outcome began to focus on reducing the late effects of treatment. Contemporaneously, surgical management of the primary tumor was being assiduously promul-

gated by authors such as Pritchard, who published retrospective analyses of prechemotherapy data which were interpreted to demonstrate an improvement in survival resulting from amputation or wide resection as initial treatment.¹⁴⁹ Pritchard also published observations indicating that patients in IESS-I had superior time to relapse and survival when surgical resection was a component of treatment. In that study, pelvic primaries were more frequently treated nonsurgically, and multivariate analysis of survival identified pelvic primary tumor as an adverse prognostic factor.¹⁵¹ Nonetheless, the nonrandomized assignment of more favorable primary tumors to surgery allowed the conclusion that surgery was at least as good as radiation in treatment of the primary site in patients with localized disease.¹⁵¹

Although randomized comparisons are lacking, local control of lesions treated with surgery alone or surgery plus radiation have been excellent. Local control rates following surgery \pm radiation average 94%. The results of several surgical resection series are summarized in Table 5.14. Disease-free survival and overall survival following resection compared favorably to results obtained with radiation. Despite selection of small, noncentral, or nonpelvic tumors which would have a good prognosis regardless of the local therapy, surgical resection in some instances may be more effective in preventing local recurrence.^{153,172} The use of lower doses of radiation following surgical resection is theoretically appealing in that late effects including second cancers might be reduced in comparison to full-dose radiotherapy.¹⁷² However, this has not been adequately assessed in prospective studies, and the routine use of both surgery and radiotherapy has been questioned.¹⁷³

Notwithstanding the excellent results for surgical resection alone or combined with radiation in highly selected patients, very good to excellent results have

been reported for induction chemotherapy followed by local radiotherapy. Local control results obtained with radiation as the local modality range from 44% to 100%, and are affected by pretreatment factors such as primary site and tumor volume, as well as treatment-related factors such as the response to chemotherapy and radiotherapy technique. The results of radiation therapy for Ewing's sarcoma are summarized in Table 5.15.

The IESS-I and IESS-II established the standard to which the results of radiation and chemotherapy must be compared. IESS-I evaluated the additions of Adriamycin and pulmonary radiation to vincristine, actinomycin, and cyclophosphamide (VAC) chemotherapy in the multimodality treatment of non-metastatic Ewing's sarcoma. Long-term results were reported for 331 patients,¹⁷¹ and radiotherapy results were reported for 271 patients.¹⁷⁴ Relapse-free survival and overall survival at 5 years were superior when Adriamycin was added to VAC compared to VAC alone ($p < 0.001$).

This study also demonstrated that pulmonary irradiation improved relapse-free and overall survival when added to VAC, compared to VAC alone ($p < 0.001$). The results of IESS-I are summarized in Table 5.16. The difference between the group treated with Adriamycin and the group treated with pulmonary radiation was less pronounced, and reached statistical significance only when all eligible randomization groups were considered.¹⁷¹ Local control for all patients was 89.2%, with no significant differences among the treatment groups.¹⁷⁴ Despite the lack of statistical significance, local control in patients with inadequate radiotherapy volumes or doses was improved by the addition of Adriamycin (90% versus 71.4%).^{168,174} Pelvic primary site and age >15 years were associated with a poor prognosis.¹⁷¹

In IESS-II, high-dose intermittent Adriamycin was compared to lower dose continuous infusion

Table 5.14 Local control following resection \pm radiation for extremity Ewing's sarcoma

Reference	Institution	No. of patients	Local control	5-year survival, DFS, RFS	Preoperative/postoperative radiotherapy	Amputation
Wilkins	Mayo	27	96% (26/27)	74%	27/27 (100%)	5/27 (18.5%)
Sauer	CESS-I	60	90% (54/60)	64%	29/60 (48%)	ND
Sailer	MGH	12	100%	92%	92%	1/12 (8%)
Hayes	StJude	11	100%	80%*	0	ND
Arai	StJude	17	100%	75%	7/17 (18%)	ND
Toni	Bologna	69	96%	59%	31/56 (55)	13/69 (19%)
Dunst	CESS-II	132	96%	70%	63/91 (69%)	(9%)
Tereki	Brown University	22	95%	41%	13/22 (59%)	4/22 (18%)
Villoreal	Chile	16	100%	50% (7-year)	50%	ND

*This survival estimate is for all treated patients. Only two relapses occurred among the 11 patients treated with surgery alone as the local treatment. ND = Not described; DFS = disease-free survival; RFS = relapse-free survival.

Table 5.15 Results of radiotherapy for Ewing's sarcoma

<i>Institution</i>	<i>Years</i>	<i>No. of patients</i>	<i>Chemotherapy agents</i>	<i>Radiation dose</i>	<i>Volume</i>	<i>Local control</i>	<i>5-year EFS/DFS</i>	<i>Reference</i>
MGH	1930–1952	22	None	2000–6000 r	WB	68%	18%	Wang <i>et al.</i> ¹
UCSF	1945–1965	20	None	16–65 Gy	WB	72%	25%	Phillips and Sheline ²
IESS-I	1973–1978	148*	VACA	55–65 Gy	WB	89%	60%*	Nesbit and Rosen ¹⁷¹
IESS-II	1978–1982	108†	VACA	55 Gy	WB	93%	73%†	Burgert <i>et al.</i> ¹⁷⁵
CESS-I	1981–1985	32	VACA	45–60 Gy	WB	54% ^a	44%	Sauer <i>et al.</i> ¹⁵⁸
CESS-II	1986–1991	44	VACA/VAIA	60 Gy	PB	86%	70%	Dunest <i>et al.</i> ¹⁷⁷
St Jude	1978–1988	43	VA/CA/BCNU	30–60 Gy	PB	58% ^b	53%	Arai <i>et al.</i> ¹⁵⁵
NCI	1968–1980	107	VC/VAC/VADRIAC	50 Gy	WB	80%	29%	Kinsella <i>et al.</i> ¹⁶³
NCI	1986–1992	46	VADRIAC/IE	26–63 Gy	N/A	80%	42%	Wexler <i>et al.</i> ¹⁶⁴
Chile	1986–1991	11	VACA	45–63 Gy	PB	73%	36%	Villareall <i>et al.</i> ¹⁶¹
Scandinavia	1984–1990	17	VACAMB	40–60 Gy	N/A	76%	35%	Nilbert <i>et al.</i> ¹⁸¹
UK	1978–1986	108	VACA	32–55 Gy	WB	69%	35%	Craft <i>et al.</i> ¹⁸⁴
Bologna	1972–1987	62	VA/VACA	35–60 Gy	WB/PB	66%	N/A	Toni <i>et al.</i> ¹⁵⁴
University of Florida	1971–1990	31	VADRIAC	50–68 Gy	WB/PB	77–81%	N/A	Bolek <i>et al.</i> ¹⁶⁶
POG 8346	1983–1988	94	AC/VAC/VACA	55.8 Gy	WB/PB	65%	41%	Donaldson <i>et al.</i> ¹⁵⁷

* Best treatment arm of IESS-I – VAC and Adriamycin

† Best treatment arm of IESS-II – VAC and high-dose intermittent Adriamycin – 43% of patients had surgical resection

^a90% of patients (17/19) with local relapse had violation of radiation protocol

^bLower doses and limited volumes were associated with reduced local control

^c16/21 (76%) of local failures occurred in patients treated with ¹³⁷Cs prior to chemotherapy

Gy = Gray; r = roentgen; PB = partial bone; WB = whole bone; VAC = vincristine, dactinomycin, cyclophosphamide; VACA = vincristine, dactinomycin, cyclophosphamide, Adriamycin; VA = vincristine, dactinomycin; CA = cyclophosphamide, dactinomycin; VAIA = vincristine, dactinomycin, ifosfamide, Adriamycin; VADRIAC = vincristine, Adriamycin, cyclophosphamide; IE = ifosfamide, etoposide; VC = vincristine, cyclophosphamide; AC = Adriamycin, cyclophosphamide; VACAMB = vincristine, dactinomycin, cyclophosphamide, Adriamycin, methotrexate, bleomycin; BCNU = bis-chlorethyl nitrosourea.

Adriamycin. All patients received four-drug chemotherapy and radiotherapy. In patients with nonpelvic primary tumors, surgical resection was encouraged by study investigators. This resulted in amputation, or resection in 43% of all patients. The radiotherapy protocol was identical to IESS-I and consisted of treatment of the entire bone to 45–55 Gy followed by a 10 Gy boost to the tumor site plus 5 cm margin. Relapse-free, disease-free and overall survival were superior with high-dose intermittent Adriamycin compared to low-dose continuous Adriamycin (73%, 68%, and 77% versus 56%, 68% and 63%, respectively; $p < 0.05$). Local control for all patients enrolled was 91%, with no significant difference in local control between the randomized groups (93% versus 90%).¹⁷⁵ Increasing awareness of the late toxicities of whole-bone radiotherapy led investigators to analyze patterns of local recurrence relative to the irradiated field. Noting that the great majority of local recurrences develop in sites identified radiographically, Suit suggested reducing the dose of radiation to uninvolved intermedullary sites when aggressive chemotherapy was to be used.¹⁷⁰

Table 5.16 Results of IESS-I (percentages)

<i>Endpoint</i>	<i>Treatment 1</i>	<i>Treatment 2</i>	<i>Treatment 3</i>
5-year recurrence-free survival	60	24	44
5-year survival	62	23	51

Treatment 1: radiotherapy to the primary lesion plus VACA (vincristine, dactinomycin, cyclophosphamide, Adriamycin).

Treatment 2: radiotherapy to the primary lesion plus VAC (vincristine, dactinomycin, cyclophosphamide).

Treatment 3: radiotherapy to the primary lesion plus VAC (vincristine, dactinomycin, cyclophosphamide) and bilateral pulmonary radiation.

The German Co-operative Ewing's Sarcoma Study (CESS) I sought to evaluate multimodality therapy for non-metastatic Ewing's sarcoma, and to test lower-dose radiotherapy treatment of the primary site. All patients received local treatment following weeks 18–20 of chemotherapy (VAC plus Adriamycin). Radiation doses were 36 Gy following resection with positive margins,

50–60 Gy for patients with unresected central/pelvic lesions, and extremity lesions were randomized to receive either 46 Gy or 60 Gy. Shrinking-field technique was used which consisted of 36 Gy delivered to the whole bone, followed by treatment of the tumor bed plus 5 cm margin to 45 Gy, and finally treatment of the tumor bed plus 2 cm margins to 60 Gy. In this study, assignment of local resection or radiation was nonrandomized and based on physician preference. Local control, disease-free survival and overall survival following resection was 97%, 65%, and 62%, respectively. For the resection plus radiation group, local control, disease-free survival, and survival at 5 years was 83%, 69%, and 66%, respectively. The results for the radiation-alone group were disappointing, with local control, disease-free survival, and survival at 5 years equal to 54%, 44%, and 28%, respectively. The worse-than-expected results for the radiotherapy arm, which were confirmed by an interim analysis, prompted centralization of radiotherapy planning and quality assurance in 1984.¹⁵⁸ Although radiotherapy results improved with better radiotherapy quality assurance (i.e. there were no further local failures), a large percentage of patients had been enrolled prior to improvements in radiotherapy planning, and these patients were not excluded from analysis of the study results. Significant prognostic factors identified in that study included a good histopathologic response to chemotherapy in the resected tumor, and tumor volumes <100 ml. There was no significant difference in the relapse rates for patients randomized to low-dose or high-dose radiation.^{158,176} The authors postulated that high local failure rates with radiotherapy alone resulted from: (a) late initiation of local therapy (week 18); (b) a larger percentage of central and proximal tumors in the irradiated group; and (c) protocol deviations which were noted in 17/19 patients who had local relapse following radiotherapy.^{158,176}

In the subsequent CESS 86 study there were several changes in protocol design which reflected the experience gained from CESS 81. These included centralized radiotherapy planning and quality assurance, earlier implementation of radiotherapy (week 9 rather than week 18) and greater utilization of surgical resection (approximately 75% of patients).¹⁷⁷ The chemotherapy regimen consisted of VAC with Adriamycin as in CESS 81, alternating with VAIA (in which ifosfamide with mesna was substituted for cyclophosphamide). The nonrandom assignment of local treatment was as follows: surgical resection alone (39 patients); surgery and radiotherapy (93 patients); radiation alone (44 patients). Forty-five gray was given following resection, and 60 Gy was given when radiation alone was used for local treatment. Patients receiving radiation were randomized to conventional fractionation or a split-

course hyperfractionated regimen. Local control following surgery, radiotherapy, and surgery plus radiotherapy was 100%, 86%, and 95%, respectively. No statistical comparison of local control rates for surgery versus radiation alone was provided. However, there were no statistical differences in relapse-free or overall survival between the surgery, radiation alone, or surgery plus radiation groups. No significant differences in the 5-year local control (82% versus 86%), relapse-free survival (53% versus 58%), or survival (63% versus 65%), were observed between conventional and hyperfractionated groups, respectively. Unlike CESS 81, tumor volume and response to chemotherapy were not significant prognostic factors. The improved results obtained in CESS 86 were primarily due to improved local control of the primary site. The improved local control was believed to result from: (a) earlier implementation of radiotherapy; (b) the use of higher doses of radiation in larger percentage of patients; (c) improved radiation technique with centralized planning; (d) the more frequent use of surgery; and (e) the more frequent use of combined surgery and radiotherapy for local treatment in patients with high risk features (i.e. pelvic primaries). Indeed, the most striking improvements were observed in patients with tumor volumes >100 ml, and in patients with pelvic primary tumors who the authors concluded should be treated routinely with combined local therapy.¹⁷⁷

More recently, Bacci *et al.* analyzed prognostic factors in 359 patients with nonmetastatic Ewing's sarcoma. The analysis includes patients treated over a 16-year period (1979–1995) with four different Adriamycin-containing chemotherapy regimens, the most recent of which employed ifosfamide as one of the induction agents. Local therapy consisted of surgery alone, radiation alone or a combination of the two. In general, only very young patients, and select patients with easily expendable primary sites, were treated surgically in earlier years, while there was a greater emphasis on routine surgical resection in later years. Radiation was routinely given to older patients following marginal resection. Univariate analysis of the entire group revealed a superior 5-year event-free survival for surgery compared to radiation (64.7% versus 47.5%). The local recurrence following surgery alone was 6% compared to 19% for radiation alone. The local recurrence and 5-year event-free survival rates were 8.5% and 55.7%, respectively for patients treated with surgery plus radiation. These results reflect, in part, the selection of patients with less favorable prognostic factors for radiotherapy. Multivariate analysis identified age >17 years, male sex, fever, anemia, elevated LDH, tumor location other than extremity,

and the chemotherapy regimen, as independent predictors of event-free survival when all 359 patients were analyzed. A second multivariate analysis confined to the 174 resected patients identified fever, anemia, serum LDH, and histologic response to chemotherapy as independent predictors of event-free survival.¹⁷⁸ Prognostic factors for Ewing's sarcoma are listed in Table 5.17.

A trial of low-dose, limited-volume radiotherapy was reported by Arai and colleagues from St Jude Children's Research Hospital.¹⁵⁵ Sixty cases of localized Ewing's sarcoma were treated with Adriamycin-containing induction chemotherapy, and alternating vincristine/actinomycin, and cytoxan/Adriamycin maintenance for 57 weeks. Radiographic complete response to chemotherapy occurred in 29/45 (64%) and objective response was noted in 37/45 (82%) of evaluable cases. Local therapy consisted of surgery in 17 patients (complete resection prior to chemotherapy in three patients, complete resection following chemotherapy in 14 patients). Three patients with positive microscopic margins received postoperative radiation (35–41 Gy). Local control for the surgically treated groups was 100% and the 5-year event-free survival was 75%. Forty-three patients received radiation as the primary local modality. In all cases, radiation fields were limited to 3 cm beyond osseous tumor or post-chemotherapy regional soft-tissue extension. Prior to 1985, low-dose irradiation (30–36 Gy) was utilized for: (a) patients having complete response to chemotherapy, (b) patients with negative post-chemotherapy biopsies, and (c) cases with no measurable soft-tissue extension prior to chemotherapy. "High-dose" (50–60 Gy) radiotherapy was utilized for all patients with progressive disease, and those with biopsy-confirmed residual disease following chemotherapy. Following 1985, high-dose radiation therapy was used for all patients with tumors > 8 cm at diagnosis. Local control and event free-survival for the radiotherapy group was 58% and 53%, respectively at 5 years. These results were significantly inferior to the surgically resected group ($p = 0.044$). Surgically resected patients consisted of a more favorable group who had smaller, nonpelvic primary tumors. Tumor diameter and response to induction chemotherapy were significant predictors of local control and event-free survival in the radiotherapy group. In the "low-dose" group, local control of tumors < 8 cm in diameter was 90% while for tumors greater than 8 cm it was 52%. A surprisingly low 5-year local control rate of 39% was reported for the "high-dose" group, although no exploration or discussion of this aspect of the St Jude experience was offered. Although the local failure rate was high, local recurrence was central within the target volume in 18/19

Table 5.17 Prognostic factors in 359 nonmetastatic Ewing's sarcoma determined by multivariate analysis (modified from ref. 178)

Variable	p-Value
Age	< 0.001
Sex	< 0.04
Fever	< 0.0002
Anemia	< 0.02
LDH	< 0.0003
Tumor site	< 0.02
Chemotherapy regimen	< 0.00003
Histologic response to chemotherapy*	< 0.00001

*Results from 179 surgically resected patients analyzed in a separate multivariate analysis from entire cohort of 359 patients.

(95%) of the cases. The authors concluded that the limited irradiation volume did not affect local control, that tumor size and response to chemotherapy were predictive of outcome, and that low-dose radiotherapy could *not* be routinely recommended regardless of the response to chemotherapy.¹⁵⁵

In another prospective study of radiotherapy technique, the Pediatric Oncology Group trial 8346 addressed whether "involved field" (IF) radiotherapy was as effective as "standard field" (SF) radiotherapy in the treatment of Ewing's sarcoma.¹⁵⁷ SF was defined as whole-bone radiation to 39.6 Gy followed by a boost to the prechemotherapy tumor volume, plus 2 cm for a total dose of 55.8 Gy. IF was defined as the tumor volume at presentation plus 2 cm. This also received a total dose of 55.8 Gy. All patients received induction chemotherapy with planned local treatment at week 14. Surgical excision was encouraged for primaries within expendable bones. A preliminary analysis in 1986 revealed a low number of patients being entered in the radiotherapy randomization due to a greater than expected number of patients presenting with either metastatic disease or small, surgically resectable localized tumors. The radiotherapy randomization was discontinued in favor of treating all patients with IF radiotherapy on study. Patients with systemic relapse underwent biopsy of the primary site if it did not appear to be involved clinically. One hundred and forty-one evaluable patients presented with localized disease. The overall response to chemotherapy was 88% and the complete response rate was 28%. Thirty-seven patients underwent surgical resection, with 16 (43%) requiring postoperative radiotherapy. The 5-year event-free survival for patients undergoing surgery was 88% and the local control for this group was 88%. The event-free survival and local control for the radio-

therapy group was 41% and 65%, respectively. Control rates differed significantly as a function of primary site. Central, pelvic/sacral, proximal, and distal extremity sites had local control rates of 82%, 44%, 69%, and 80%, respectively ($p = 0.02$, log rank). There was no difference in local control for IF (53%) and SF (53%) radiotherapy. The quality of radiotherapy technique was significantly associated with local control. Patients treated without any deviation from the radiotherapy protocol enjoyed an 80% local control rate, while those with minor and major radiotherapy protocol violations had local control rates of 48% and 16%, respectively ($p = 0.005$). Analysis of the pattern of local failure revealed recurrence within the irradiation volume in 18/29 (62%) cases, and outside of the irradiated volume in 7/24 (24%). The reported chronic toxicities consisted of three second bone sarcomas, one of which arose in a nonirradiated bone, and orthopedic complications in 39% of surgically resected patients.¹⁵⁷ An example of "tailored field" radiotherapy for a Ewing's sarcoma of the distal femur is shown in Figure 5.9.

The above two studies, which explore reduced radiation dose and volume in the treatment of the primary site, highlight the critical importance of adequate radiotherapy technique and the attention to detail required to cure Ewing's sarcoma with radiotherapy. In the St Jude experience, local failures in the low-dose radiotherapy groups occurred within the tumor bed in 18/19 cases. While this may indicate that a "limited volume" of 3 cm margin on osseous and soft-tissue extent of tumor was an adequate volume to treat, it is quite possible that the central local failures resulting from "low-dose" (30–36 Gy) radiotherapy may have prevented detection of marginal or out-of-field failures which may have become clinically evident with more durable central control.¹⁵⁵ Indeed, with higher prescribed tumor doses and "tighter" margins, 24% of local failures were outside of the irradiated volume in the POG trial.¹⁵⁷ It should be noted that the lowest local control rates were obtained for pelvic primary sites, where tumors are typically large and doses of >60 Gy have been used with some success.¹⁷⁹ It is possible that the percentage of marginal recurrences may have increased with higher local doses in those patients with pelvic primary sites.¹⁵⁷

From these studies it can be assumed that doses <55 Gy and radiotherapy margins <4–5 cm should not be routinely used outside of well-planned clinical trials when radiotherapy alone is to be relied upon for local cure of Ewing's sarcoma. The radiotherapy target volume should be defined only after meticulous review of MR, CT and plain-film studies with a musculoskeletal radiologist and orthopedic oncologist. With regard to postoperative radiation for close or positive

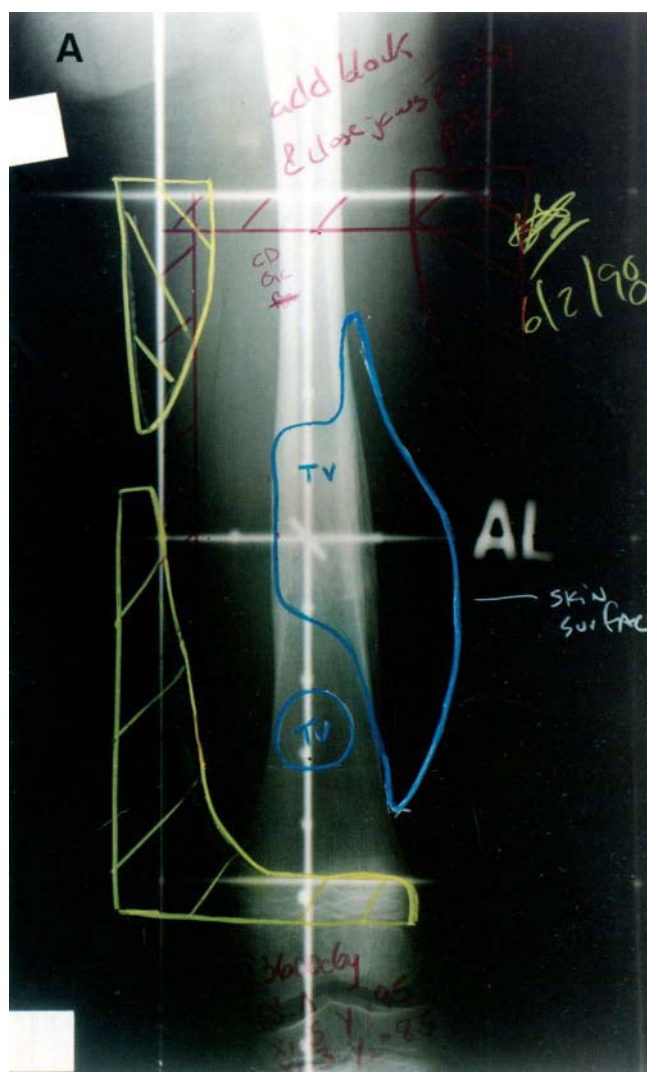


Figure 5.9 (Continued on next page)

margins, there are no data in the Ewing's sarcoma or radiotherapy literature which suggest that the prescribed dose of radiation can be determined by the pathologic response in the resected specimen, despite reports that the pathologic response (extent of necrosis) in the resected specimen predicts disease-free survival.^{158,176,180,181}

Pelvic Ewing's

Pelvic primary tumors have been associated with a poor prognosis.^{155–157,162,168,171,174,182–189} This has been attributed to a delay in diagnosis resulting in more locally advanced primary tumors with a higher propensity for metastatic relapse.^{182,190} Local control of bulky pelvic Ewing's is particularly challenging, and the superiority of either surgery, radiotherapy or combined treatment remains controversial.

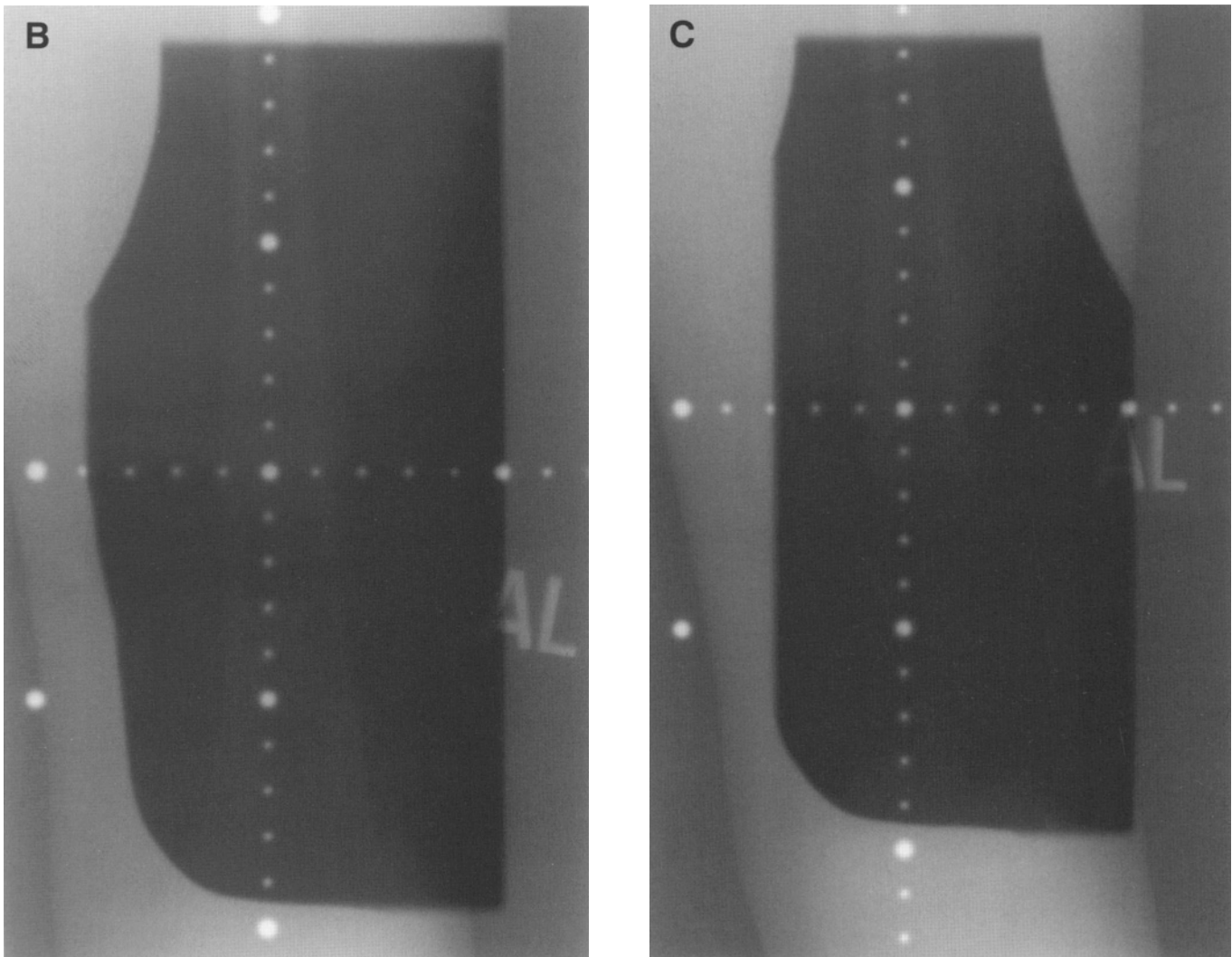


Figure 5.9 (continued from previous page) Tailored field radiotherapy for Ewing's sarcoma of the distal femur. The anterior simulation film is shown in (A). The bone and soft-tissue components of the pre-chemotherapy tumor volume (TV) are treated with 2–3 cm margin. After 3600 cGy the field is "coned down" with additional blocks and a reduction in field size to limit the coverage to the TV plus 2 cm. A port film of the initial field is shown in (B), and a port film of the "cone down" field is shown in (C).

The IESS-I experience with Ewing's sarcoma of the pelvic bones was reported initially by Evans *et al.*¹⁸² Sixty-two patients with non-metastatic Ewing's sarcoma of the pelvis were randomized to receive VAC, VAC plus Adriamycin, or VAC plus bilateral pulmonary irradiation. The median time to relapse for pelvic primaries on IESS-I was 92 weeks compared to 222 weeks for nonpelvic lesions ($p = 0.002$). In contrast to nonpelvic primaries, there was no difference in the rate of metastatic relapse between treatment regimens for patients with pelvic primaries. There was no relationship between local control and radiation dose (4000–6000 cGy) or field size (less than or greater than 5 cm margin). Local control was not significantly

improved in the 11/62 (18%) of patients treated with complete resection (82%) compared to those treated with biopsy and radiotherapy (72%). Local control and time to relapse were decreased for all lesions 10–15 cm in diameter compared to those <5 cm. Fifty percent of pelvic lesions were 10–15 cm, in contrast to only 34% of lesions at other sites treated on IESS-I. In the long-term follow-up report of the IESS-I study, Nesbit *et al.* reported 5-year survival of 34% for pelvic sites compared to 57% for nonpelvic sites ($p < 0.01$). Similarly, there was no difference in survival by treatment regimen for pelvic primaries, in contrast to nonpelvic primaries, for which the addition of Adriamycin improved survival ($p < 0.01$).¹⁷¹

In response to the higher rate of metastatic relapse and local recurrence in IESS-I, all patients with pelvic primaries were treated with high-dose intermittent chemotherapy containing Adriamycin and surgical resection whenever possible in IESS-II. Unlike IESS-I, CT scanning was routinely employed for radiotherapy treatment planning. The results were significantly superior to IESS-I. The local recurrence rate of pelvic primaries was 12% for IESS-II compared to 28% for IESS-I ($p = 0.03$). The rate of metastatic relapse was significantly reduced in IESS-II (37%) compared to IESS-I (67%, $p = 0.004$). The 5-year relapse-free survival and overall survival were 55% and 63% for IESS-II versus 23% and 35% for IESS-I respectively ($p = 0.002$). Surgically resected patients had fewer local recurrences (1/19), than did patients treated with biopsy only and radiation (6/39). A statistical comparison of local control for resected and nonresected patients was not provided. However, there was no difference in relapse-free survival or overall survival between resected and nonresected patients. The authors concluded that the increased use of resection, along with better radiotherapy and more intense chemotherapy, achieved their goal of improving survival in patients with pelvic Ewing's sarcoma.¹⁹¹

Despite the encouraged use of resection and the improved outcome on IESS-II, the benefit of resection in patients with pelvic Ewing's sarcoma has yet to be proven in a randomized trial. Single-institution retrospective analyses from Memorial Sloan Kettering and Mayo Clinic suggest that resection improves outcome. Li *et al.* reported improved survival associated with surgical resection and contemporary chemotherapy in 10 patients, compared to eight patients treated with an earlier chemotherapy regimen and radiotherapy. Three of the 10 patients in the radiation group developed metastatic disease, compared to only one patient in the resected group. The authors admitted that the improved outcome was in part a result of improved chemotherapy. Unfortunately, the contribution of resection could not be assessed in this study due to the selection of more favorable patients in the surgery group who received more modern chemotherapy.¹⁹²

Frassica *et al.*¹⁹³ detailed the Mayo Clinic experience with Ewing's sarcoma of the pelvis. Twenty-seven patients were reviewed, six with metastatic disease at diagnosis. Eight patients had resection with or without radiation and chemotherapy and 13 patients had chemotherapy and radiation. Four of 13 (30%) patients developed a local recurrence with or without metastatic relapse in the radiotherapy group and the actuarial local relapse rate was 44%. In the resection group, 50% underwent hemipelvectomy (three formal hemipelvectomies and one internal hemipelvectomy).

Postoperative radiotherapy was used in 50% of resected patients. Local recurrence and death from metastatic disease occurred in one patient following hemipelvectomy, and metastatic recurrence developed in one patient who received an internal, then formal, hemipelvectomy. The actuarial 3- and 5-year survival rates were both 75%, and the actuarial local control rate was 88% for the resected lesions. Although resected patients did better, selection bias and treatment differences prevent any conclusions regarding the superiority or resection in that study.¹⁹³

A series of 39 patients with pelvic Ewing's sarcoma from Boston Children's Hospital and the Massachusetts General Hospital was reported by Scully and colleagues.¹⁸⁹ All patients were treated with various chemotherapy regimens used throughout the study period of 1975–1991. Local treatment consisted of radiation alone in 20 patients, surgery alone in three patients and resection plus radiation in 16 patients. All surgically treated patients (19) were compared to those treated with radiation-alone (20) patients. Twelve patients presented with metastatic disease; eight received radiation alone and four were treated with surgery \pm radiation. Local failure occurred in six patients; three following resection (local control = 16/19, 84%) and three following radiation (local control = 17/20, 85%), with no difference between the two groups ($p = 0.96$). Patients with metastatic disease at presentation had shorter median survival (25 months versus 44 months, $p = 0.013$). There was a trend for longer relapse-free survival in resected patients (22 months) compared to those treated locally with radiation alone (16 months, $p = 0.336$). Similarly, there was a longer median survival for the resected group (42 months) compared to the radiation group (25 months), although this difference was nonsignificant ($p = 0.13$). The overall survival for all 39 patients was only 38%, perhaps reflecting the influence of metastatic disease at presentation in 30% of the study cohort. The authors concluded that a resection was not associated with a significant disease-free advantage despite the inherent bias favoring the resected group. Indeed, the percentage of patients with metastases at presentation in the radiation group was twice that of the resected group (40% versus 20%), and a subgroup analysis excluding metastatic patients was not provided. Notwithstanding, the local control rates were virtually identical for resected and irradiated groups.¹⁸⁴ A lack of significant difference in outcome between irradiated and resected patients with pelvic primaries was also reported by Evans for IESS-II patients, and by Bacci *et al.*^{188,191}

The available data justify the use of resection of pelvic sites when functional morbidity and disfigurement will

be minimal or non-existent. In doing so, surgical resection of the primary site augments local control, and reduces the patient's risk of suffering a radiation-induced bone sarcoma at the primary site. However, with appropriately aggressive chemotherapy and well-planned radiation, local control rates exceed 80%, and the risk of second cancer at 15–20 years equals 3–7%.^{194,195} Since systemic relapse is at least 3 times as likely as local failure in patients with pelvic Ewing's sarcoma, advances in systemic treatment will have greater impact on survival than improvements in local therapy. However, given the ominous prognosis of local failure, optimization of local therapy remains the second most important goal in the management of pelvic Ewing's sarcoma. A randomized trial, as proposed by Horowitz *et al.*,¹⁹⁶ is needed to prove any incremental improvement of disease-free or overall survival afforded by resection.

Radiation-induced Sarcoma Following Treatment of Ewing's Sarcoma

Ewing's sarcoma patients appear to be at an increased risk for radiation-associated bone and soft-tissue sarcomas in comparison to other solid tumors of childhood – their risk being second only to children with bilateral retinoblastoma.^{194,197} Although the reported cumulative incidence of radiation-induced sarcoma varies from 5.5% to >35% at 20 years,^{195,197–199} there is agreement among reports that the risk of a radiation-induced sarcoma increases with time and radiation dose.^{195,197,199} In an early report from the late-effects group, Tucker *et al.* reported a 20-year incidence of 22.1% for patients who received radiotherapy for Ewing's sarcoma. Their analysis revealed that doses >60Gy, and increasing exposure to alkylating agents, significantly potentiate the risk of radiogenic bone sarcoma.¹⁹⁷

Kuttresh and colleagues from the NCI, St Jude's and the University of Florida at Gainesville reviewed 266 survivors of Ewing's sarcoma, all of whom had received radiation with or without chemotherapy. Sixteen patients developed a second malignancy with a median latency period of 7.6 years. Ten of the 16 malignancies were sarcomas (five osteosarcomas, three fibrosarcomas, and two malignant fibrous histiocytomas). All second solid malignancies occurred at the primary site or within the irradiated volume. The median radiation dose received in the 10 patients was 61.1 Gy (range 50–64 Gy). The remaining six neoplasms included acute lymphoblastic leukemia, acute myeloblastic leukemia, meningioma, basal cell carcinoma, bronchoalveolar carcinoma and carcinoma-*in-situ* of the cervix. The patients who developed meningioma, basal cell carcinoma and bronchoalveolar carcinoma had received local

radiotherapy to the sites of the second neoplasm, or had received total-body irradiation (bronchoalveolar carcinoma). The cumulative incidence of a second neoplasm was 5% and 9.2% at 10 and 20 years postdiagnosis, respectively. For secondary sarcoma the cumulative estimated incidence rates were 3% and 6.5% at 5 and 10 years postdiagnosis. A dose-response relationship was reported for the risk of secondary sarcoma. The absolute risk of secondary sarcoma was zero for patients who received <47.99 Gy, 24.9 cases per 10,000 person-years for doses between 48 and 59.9 Gy, and 131 cases per 10,000 person-years for those receiving doses ≥ 60 Gy. These are approximately equivalent to 5% at 20 years for doses between 48 and 59.9 Gy, and 21% at 20 years for doses ≥ 60 Gy. In this pooled data set more secondary sarcomas occurred in patients treated at the NCI where higher doses were used more routinely.²⁰⁰

The risk of osteosarcoma in 4257 survivors of childhood cancers in France and Great Britain who presented with tumors other than osteosarcoma was recently analyzed by Le Vu and colleagues. The 20-year cumulative incidence of second osteosarcoma was 6.7% following treatment of Ewing's sarcoma. The risk of osteosarcoma was radiation dose-dependent, and the relative risk per unit dose was lower among Ewing's sarcoma patients, suggesting the possibility that genetic predisposition may contribute to the development of second osteosarcomas in patients with primary Ewing's sarcoma.¹⁹⁴

Finally, Dunst *et al.* recently reviewed the CESS 81 and CESS 86 database for second malignancies following treatment of Ewing's sarcoma. Eight second malignancies were reported in a cohort of 640 patients. There were four leukemias, one myelodysplastic syndrome, one osteosarcoma, one fibrosarcoma, and one malignant fibrous histiocytoma. All three second solid malignancies occurred in irradiated patients and were located partially or completely within irradiation volume. The risk of developing any second malignancy was 4.7% at 15 years, and the risk of a second solid malignancy was between 3% and 6% following radiotherapy at 15 years. Three out of five patients with leukemia died of rapid progression. In contrast, two out of three patients with second solid malignancies were salvaged with surgery and chemotherapy, and are alive without disease 4.3 and 7.5 years following diagnosis.¹⁹⁵ Despite reports of second sarcomas developing in >35% of survivors at 20 years,¹⁹⁹ the risk of a radiation-induced second sarcoma in more contemporary cohorts of Ewing's survivors is between 3% and 7% at 20 years when doses below 60 Gy are used.^{194,195,200,201} Since the risk of second sarcoma is time- and radiation dose-dependent, additional follow-up is needed to more

adequately assess the incidence of second sarcoma in modern cohorts. Existing data suggest that the risk of second cancer increases significantly when doses >60 Gy are used.

OSTEOSARCOMA

Extremity

The past 30 years have witnessed dramatic improvements in the treatment and survival of patients with osteosarcoma. Multiagent chemotherapy regimens which include high-dose methotrexate, doxorubicin, cisplatin, and ifosfamide have been shown in single-institution^{202–207} and cooperative trials^{208,209} to significantly prolong survival. Chemotherapy has also demonstrated its ability to sterilize tumor at the primary site. This finding, which is of prognostic importance,^{202,210} provides an intuitive reassurance regarding limb-salvage surgery, as well as information which can be used to optimize adjuvant chemotherapy.²¹¹ The ability of chemotherapy to improve local control, combined with the dramatic improvements in surgical techniques and prosthetics, has allowed limb- and/or function-sparing surgery following neoadjuvant chemotherapy to be offered to the majority of patients with improved results.^{203,212} The role of radiotherapy in the routine management of extremity osteosarcoma is virtually nonexistent today. However, radiotherapy has been reported to improve local control of borderline or unresectable extremity osteosarcoma, vertebral osteosarcoma and pelvic osteosarcoma.^{66,70,73,74,121,213,214} It has also been used to successfully treat osteosarcomas of the mandible.^{215–218} Due to space limitations, treatment of craniofacial osteosarcoma with radiation will not be discussed, and the reader is referred to an excellent recent review.²¹⁹ High-LET radiotherapy, preoperative radiotherapy and radiation sensitizers have been used successfully for treatment of osteosarcoma.^{72,121,220,221}

Radiotherapy was originally proposed by Ferguson²²² and again by Cade²²³ in the 1950s as means of local treatment which might alleviate symptoms and delay amputation in the patient presenting with localized disease, so as to allow occult metastases to declare themselves, thus enabling the avoidance of a non-curative amputation. Radiation doses of 70–90 Gy were delivered in 8–12 weeks followed in 6–9 months by amputation.²²³

This strategy was implemented in 23 patients reported by Phillips and colleagues at the University of California San Francisco. Treatment consisted of preoperative radiation (50–100 Gy) and amputation. When compared to 11 patients treated with amputation alone there was no significant difference in survival. In

six cases no viable tumor was seen at amputation, and all but one of the six had received 100 Gy.² Allen and Stevens compared preoperative radiation (79–100 Gy) in 10 patients to 20 patients treated with surgery alone, and claimed a survival advantage at 5 years (60% versus 10%) in favor of preoperative radiation.²²⁴ In an early Princess Margaret experience, preoperative radiation was administered to 29 patients, 27 of whom were evaluable. No patients received >80 Gy, and three patients were treated under conditions of hypoxia. All 27 evaluable patients locally recurred after a mean duration of only 3.6 months. The authors concluded that preoperative irradiation failed to provide durable palliation, did not allow identification of those who could be spared amputation, nor did it prolong survival.²²⁵ In addition, single- and multiple-institution studies^{226–229} demonstrated improved response rates and superior disease-free survival with the use of chemotherapy, allowing many to conclude that delaying surgical resection (and postoperative chemotherapy) in order to administer radiotherapy was contraindicated. The substantial responses to chemotherapy, and the delay in resection required to construct an orthopedic prosthesis, led Rosen and colleagues to advocate preoperative, or neoadjuvant, chemotherapy^{202,211}. Local control with this approach in the current era of en-bloc resection and limb-salvage procedures has been excellent.^{70,202,203,230}

Preoperative radiation combined with intra-arterial infusions of radiation sensitizers or chemotherapy agents has been described by several investigators.^{66,70,73,121,230–233} This treatment strategy has been described by Eilber *et al.* in a series of reports.^{66,70,230} In their initial reports Adriamycin 30 mg/day was infused over 24 h on three consecutive days followed by 3500 cGy given in 10 fractions of 350 cGy. This was followed by limb-sparing resection 7–14 days later. There were only two local recurrences in the 83 skeletal sarcomas which included 57 high-grade intermedullary osteosarcomas. Complications observed in bone sarcoma patients were frequent and usually resulted from failure of the cadaver allografts used for limb reconstruction.^{66,70}

Wiley *et al.* treated two cases of extremity osteosarcoma with preoperative intra-arterial Adriamycin and radiotherapy to 70 Gy and 80 Gy, respectively. Resection, which was performed out of concern over progressive calcification within the treated lesion, revealed extensive necrosis. However, both of these patients died of pulmonary metastases.²³¹ Enton *et al.* treated nine patients with osteosarcoma using preoperative treatment similar to the UCLA regimen. Intra-arterial Adriamycin was infused over 3–5 days followed by 300 cGy given in 10 fractions. Limb-sparing resection was performed 7–14 days later.

Pathologic analysis revealed varying degrees of necrosis with varying degrees of viable tumor present in all specimens. There were no recurrences of osteosarcoma although follow-up was limited (9–24 months, median 16 months).²³² Goodnight and colleagues treated six patients with osteosarcoma using the UCLA regimen. All were locally controlled. Two patients with bone sarcomas required amputation as a result of wound-healing complications. The overall complication rate was 38–41%.⁷³ Similar results were reported by Wanebo *et al.*⁷⁴

The intra-arterial delivery of the radiation sensitizer bromodeoxyuridine (BUDR) followed by hypofractionated radiation for osteosarcoma was reported by Martinez and colleagues at Stanford. Nine patients with unresectable primary tumors received intra-arterial infusion of BUDR, 48 h prior to 600 cGy. Treatment was given every 5 days to a total dose of 42–48 Gy. All patients also received multiagent chemotherapy every 3 weeks starting with initiation of treatment. Local control was achieved in 7/9 (78%) patients. Metastatic disease developed in 5/9 (55%) patients. Five of nine patients (55%) developed severe postirradiation fibrosis, requiring amputation in two patients. There was no viable tumor identified at pathologic analysis in the two cases treated with amputation.¹²¹ Lejeune *et al.* treated 11 osteosarcoma patients with the Stanford regimen of intra-arterial BUDR and hypofractionated radiotherapy. Ten were evaluable for response. Local control was achieved in 9/10 cases. However, severe fibrosis developed in 83% of cases, and 6/9 patients (67%) developed severe fibrosis of the knee resulting in permanent flexion.²³³

Pelvic Osteosarcoma

Pelvic osteosarcomas are rare, constituting approximately 10% of all osteosarcomas.²³⁴ The prognosis of pelvic osteosarcomas is often poor due to their large size at diagnosis. Involvement of joints, extension to other bones, microscopic invasion of normal muscle or pelvic organs, and extension into lymphatics and major pelvic veins are frequent findings.²¹⁴ In the University of Florida experience of 25 patients, 20 had primary tumors >10 cm and over half were >15 cm. Surgical resection was attempted in 18 patients. Of the 10 patients who underwent hemipelvectomy, in only two were widely negative margins obtained, and of the eight patients who had a limb-salvage procedure, in only two were histologically negative margins achieved. In 14 of the 18 operated patients margins were either wide and contaminated, marginal, or intralesional. Twelve of the involved margins resulted from extension of tumor to multiple adjacent pelvic bones or vertebral bodies. Intraluminal venous extensions of

tumor were documented in nine operated cases. Of the five patients who survived >5 years, all received postoperative local radiotherapy, and two remained locally controlled. Only one patient out of the series of 25 was a long-term survivor. The authors recommend the use of adjuvant chemotherapy and local radiotherapy despite the fact that neither has been *proven* to increase survival for patients with pelvic primary tumors.²¹⁴

Estrada-Aguilar and colleagues treated five patients with osteosarcoma of the pelvis (three primary, two metastatic recurrent) using intra-arterial cisplatin and radiation. Local control was achieved in all five patients, with two surviving 56 and 77 months, respectively.²³⁵ Hoekstra and colleagues treated five pelvic osteosarcoma patients with hemipelvectomy and IORT (20–30 Gy). Four out of five were locally controlled and two of five (40%) were long-term survivors. Complications due to IORT were limited to coccygeal necrosis in one out of five patients. Local control was superior when compared to surgery alone in a group of six historical controls.^{236,237} Finally, four patients with pelvic osteosarcoma were treated with neoadjuvant chemotherapy, photon radiation and a neutron boost at the Center Leon Berard and the Orleans Neutron Therapy unit in France. With a median follow-up of 24 months (range 22–40 months) all are alive without local recurrence or metastatic disease. Low patient numbers and short follow-up prevent conclusive observations. However, the results to date are promising.²³⁸ In summary, the frequent close or positive margins resulting in high local relapse rates following surgery and chemotherapy, and the apparent benefit of adjuvant radiotherapy^{235–238,240,242,243} indicate that innovative local treatments such as IORT, brachytherapy, intensity modulated radiotherapy (IMRT) or charged-particle therapy deserve further evaluation in these difficult tumors. While not proven, the role of adjuvant radiotherapy for pelvic osteosarcoma is supported by the literature.

Palliation

Radiotherapy can be utilized for palliation of metastatic osteosarcoma, and as an adjuvant to surgical resection at sites where wide margins are difficult to achieve. A consistent dose and fractionation regimen which is effective in palliating pain from primary and metastatic osteosarcoma is not readily apparent in the literature. Ten patients with osteosarcoma of the extremities received 10,000 cGy preoperatively at the University of Oregon. Seven of eight patients had successful palliation of pain in response to radiation.²²⁴ Rosen and Martinez, at Memorial Sloan Kettering Hospital, treated

patients with metastatic osteosarcoma with combination therapy consisting of high-dose methotrexate, Adriamycin, cyclophosphamide and radiation. Radiotherapy was usually given in three high-dose fractions (400–800 cGy) in 1 week followed by 2000 cGy in 10 fractions. Six of seven treated lesions responded completely. Two patients with spinal cord compression from osteosarcoma responded to chemotherapy and four or five fractions of 400 cGy, followed by four fractions of 200 cGy. While the relative contributions of chemotherapy and radiation to the observed responses are not clear, this experience establishes a precedent for hypofractionation in the palliative treatment of metastatic osteosarcoma.²⁴¹

Vertebral osteosarcoma has been associated with a poor prognosis even following resection and radiotherapy. Although treatment results have improved with chemotherapy, local recurrence is the major cause of treatment failure. Sundaresan and colleagues reviewed 24 patients with osteosarcoma of the spine treated at Memorial Sloan Kettering Cancer Center. Thirteen patients underwent limited resection and postoperative radiotherapy (30–45 Gy), and 11 patients treated more recently received neoadjuvant chemotherapy, and complete gross excision. Nine of 11 "recent" patients received radiotherapy, two of whom were treated with particle-beam therapy to doses of 70 cobalt Gray equivalents. There were no long-term survivors in the early cohort of 13 patients, while there were three patients who survived >5 years in the "recent" cohort, two without disease. Of the five "long-term" survivors (36–66 months), all had received local radiotherapy. The authors recommended external-beam radiation (combined photon and particle-beam) to improve local control.²¹³

Neutrons and Charged Particles

Charged-particle (protons, neon) and neutron irradiation have been evaluated as local therapy for osteosarcoma.^{244–249} Lindstadt *et al.* reviewed 19 patients treated at UCSF/Lawrence Berkeley Laboratory with neon ion radiotherapy for bone sarcoma. Three out of four patients with macroscopic osteosarcoma were locally controlled. The 5-year actuarial local control for all patients with macroscopic bone sarcoma was 59%^{244,245} Proton-beam radiotherapy alone, or combined with conventional photon therapy, was utilized to treat difficult paraspinal osteosarcomas at the Massachusetts General Hospital. Eleven out of 15 patients (73%) were locally controlled. All patients except one also received chemotherapy, and seven out of 15 had died at the time of the report, for a 5-year survival of 44%, which decreased to approximately 20% at 6 years due to intercurrent and metastatic disease.¹¹⁶

Early reports of the results of neutron radiation for osteosarcoma were poor, with only one out of nine (11%) locally controlled at the Medical Research Council Cyclotron in Edinburgh²⁴⁶ and only two out of nine (22%) locally controlled at Fermilab.²⁴⁷ Laramore and co-workers, who later summarized the results of neutron radiotherapy for osteosarcoma for six neutron facilities in the US and overseas, reported an average local control rate of 55% (40/73).^{248,249} Similar results were reported from Germany²⁵⁰ and from a review of the world experience by Wambersie *et al.*, in which 54% (52/97) were locally controlled.²⁵¹ With the development of less expensive, and more practical, hospital-based neutron and charged-particle capabilities, treatment of unresectable osteosarcoma with high-LET radiation will be increasingly offered to patients as a component of combined-modality regimens.

Pulmonary Irradiation

The lungs are the most frequent site of osteosarcoma relapse (90%) with or without adjuvant chemotherapy.²⁵² Experience with adjuvant pulmonary radiation has been conflicting and, for the most part, negative. Newton and Barrett delivered prophylactic pulmonary irradiation (1950 cGy) to 14 patients who were also treated with 6000 cGy radiation to the primary lesion. Patients who remained free of pulmonary metastases underwent amputation 6–9 months later. Six of the 14 patients were alive at > 4 years. The outcomes of these patients appeared superior to 14 historic controls treated by Cade without pulmonary irradiation.²⁵³ However, a randomized trial from the Mayo Clinic published 2 years earlier found no difference in time to development of pulmonary metastases or survival between the group assigned to receive 1500 cGy prophylactic lung irradiation and local treatment, or local treatment alone.²⁵⁴

The EROTC O2 study randomized 86 patients to receive 17.5 Gy adjuvant radiation to both lungs following radical treatment of the primary tumor. The group treated with lung irradiation had a superior metastasis-free survival (43% versus 28%, p -value = 0.06). For patients under 17 years of age the difference in metastasis-free survival was significant (48% versus 28%, p = 0.028 with a one-tailed test of significance). There was no significant difference in survival when all randomized patients were compared at 5 years (55% with lung irradiation versus 40% without, p = 0.18).^{255,256} A subsequent three-arm randomized EROTC trial comparing lung irradiation, chemotherapy, and combined lung irradiation plus chemotherapy, was reported by Burgers *et al.* in 1988. Overall survival for all patients on study was 43% at 4 years. A comparison

of the treatment arms revealed no significant difference in disease-free, metastasis-free or overall survival. The authors concluded that bilateral lung irradiation and adjuvant chemotherapy had an equal, albeit limited, benefit in patients with extremity osteosarcoma, although pulmonary irradiation was less toxic.²⁵⁷ The modest 4-year disease-free survival of 28% achieved for all patients on study is clearly inferior to that reported by other investigators.^{202,203,212} This fact, combined with the possibility of radiation-induced second cancers, has dulled interest in adjuvant pulmonary irradiation of osteosarcoma. There continues to be interest in adjuvant pulmonary irradiation among investigators of Ewing's sarcoma who earlier¹⁷¹ and more recently have shown that it prolongs disease-free survival.²⁵⁸

CHONDROSARCOMA

Chondrosarcomas have been treated successfully by a variety of radiotherapy techniques.^{108,220,239,259–264} The Princess Margaret experience with megavoltage X-ray therapy for 31 patients with chondrosarcoma was reported by Harwood *et al.* The cohort of patients treated between 1958 and 1976 was believed to represent a relatively poor prognosis group, with 11 out of 31 (35.5%) arising in the pelvis, and 12/31 (39%) having poorly or de-differentiated histology. Six of 12 (50%) patients with well, moderately or unknown differentiation treated with curative intent were locally controlled for 3.5–16 years. This is in contrast to the two out of eight (25%) patients with poorly differentiated, or de-differentiated lesions who were locally controlled following radical radiotherapy (35–82.50 Gy, average dose 51 Gy). The authors concluded the following: (a) chondrosarcoma of bone is not radioresistant; (b) gross residual tumor can be permanently locally controlled with radiotherapy; (c) doses ≥ 50 Gy are needed to control chondrosarcoma; and (d) de-differentiated and undifferentiated chondrosarcomas have a distinctive natural history, with the majority of affected patients dying of metastatic disease. They recommended radical radiotherapy for unresectable tumors, for gross microscopic residual disease following resection, and for recurrent tumors following local excision.²⁵⁹

McManey and colleagues reviewed 20 patients with chondrosarcoma treated at MD Anderson Hospital with megavoltage photons and/or neutrons. Tumors arose in the pelvis in 13 patients, vertebral body in four, distal femur in two and maxillary antrum in one. Five of 11 (45%) patients treated with radiotherapy alone were alive without progression of local disease at 12–87 months (median 30 months). The overall survival for this group of patients was 54% at 30 months. Two of

three patients who received postoperative radiotherapy were alive without recurrence at 44–52 months, and two of three patients treated primarily with chemotherapy and radiotherapy were without evidence of progressive disease at 15 and 29 months. Two of three patients treated with radiotherapy for recurrence following excision were without evidence of progressive disease at 19 and 77 months. In total 11 out of 20 (55%) of patients treated with curative intent who received photons and/or neutron irradiation with or without chemotherapy were locally controlled with a median follow-up of 30 months. Overall survival for the group was 65% (13 out of 20). In those patients treated primarily with radiotherapy, all four patients treated with combined photons and neutrons were locally controlled compared to only 1/7 patients treated with photons alone. The authors concluded that additional patients and longer follow-up is needed, since local persistence or recurrence of tumor was noted at times ranging from 26 to 156 months.²⁶⁰ In a review of the world experience, Schmitt and Wambesie reported "persisting" local control of 56% (23 out of 41) for chondrosarcoma following fast neutron radiotherapy.²⁶¹

Investigators from the Lawrence Berkeley Laboratory and UCSF reported the results of charged-particle (helium or neon) irradiation for 24 patients with chondrosarcoma or chordoma at paraspinal sites. Nineteen had gross subtotal resection, two had gross complete resection, and three had biopsy only. Chondrosarcomas received a mean dose of 65 Gray-equivalent (GyE), and chordomas received a mean dose of 72 GyE. The projected 3-year actuarial local control for the chondrosarcoma was 83%, and the 3-year survival was 69%. For the combined group of chordomas and chondrosarcomas 13 out of 24 patients failed locally. Previous recurrence, length of overall treatment, and larger tumor volumes were associated with higher rate of local failure.²⁴⁵

In the Massachusetts General Hospital experience with proton therapy for low-grade chondrosarcoma and chordoma of the skull base, 61 out of 68 (90%) were locally controlled. The 5-year actuarial disease-free survival was 76%. It was concluded that locally aggressive tumors adjacent to critical structures could be treated more effectively with protons which have a very sharp dose fall-off outside of the target volume.^{262,263} A more recent update of the Massachusetts General Hospital proton experience with "challenging" chondroid tumors of the axial skeleton (excluding tumors for the cervical spine or base of the skull) was reported by Hug and colleagues. Six patients with chondrosarcoma were treated with doses ranging from 70.2 to 77.9 cGyE. Four patients

received radiation postoperatively, and two patients were treated with gross residual disease. The 5-year local recurrence-free survival for chondrosarcomas in this series was 100%.¹¹⁶ In summary, the literature clearly indicates that radiotherapy is beneficial in the treatment of locally recurrent, unresectable or incompletely resected chondrosarcoma. These tumors should no longer be considered "radioresistant".

CHORDOMA

Chordomas are rare tumors involving the sacrum (55%), base of skull (35%) and axial skeleton (15%). They are believed to arise from remnants of the notochord.²⁶⁴ They are renowned for their relentless ability to recur locally. Radiotherapy has been used to palliate symptoms, to improve local control postoperatively, and for primary treatment of unresectable or locally recurrent tumor.^{264–270} Metastases from chordoma usually occur late in the course of disease, and may occur more frequently with vertebral primaries.²⁶⁴

Radiotherapy of chordoma has never been shown to benefit survival in a prospective study. Retrospective series suggest that radiotherapy is effective in palliation of local symptoms and may delay the time to local failure. Reddy *et al.* at the University of Kansas described 10 patients with chordoma. Eight out of 10 were treated with biopsy or resection and radiotherapy, and two were treated with surgery alone. Both of the patients treated with surgery alone failed locally, compared to 4/8 patients treated with radiotherapy. Six of 10 patients died of recurrent disease: five out of six with local recurrence, and one patient died of distant metastasis. The average time to recurrence following surgery and radiation was 4 years compared to 2.5 years following surgery alone. The 5-year disease-free survival was 33%.²⁶⁵

Saxton reported results for 19 patients with chordomas treated at MD Anderson. All four patients who received surgery alone suffered local persistence or recurrent tumor. Six patients were treated with radiotherapy alone and all recurred locally, although the time to recurrence was longer than in the surgery-alone group. Three of nine patients who received surgery and postoperative radiotherapy were without recurrence at 36, 72 and 80 months. The authors noted that neither surgery nor radiotherapy alone was locally curative. They suggested long-term follow-up was needed to adequately determine the success of treatment due to the risk of late local and distant relapse.²⁶⁶

The Princess Margaret experience with megavoltage radiotherapy for chordomas was reported by Cummings *et al.* Twenty-four patients were referred for radiotherapy between 1958 and 1974. The majority of

patients were treated with cobalt teletherapy, and the number of patients treated prior to the availability of CT treatment planning is not disclosed. A variety of radiotherapy doses and fractionation schemes were used. There were no differences in survival based on sex, location (i.e. cervical versus sacrococcygeal) or extent of surgical resection. All patients who presented with pain as the major symptom experienced relief following irradiation, with a median duration of pain relief equaling 3.5 years. Eight patients received a second course of palliative radiation to previously treated primary sites. Six of the eight patients experienced improvement or stabilization of symptoms. Overall, a total of seven patients out of 24 were without "active chordoma" at last follow-up. The authors concluded that moderate radiation doses (40–55 Gy) are sufficient to produce symptomatic relief when conventional fractionation is used.²⁶⁷

In a series of 21 patients treated at the Malinkrodt Institute from 1949 to 1986, surgery with or without radiation was associated with a survival advantage compared to radiation alone for patients with chordoma. Surgery plus radiation produced longer disease-free survival compared to surgery alone for lumbosacral chordoma (5-year: 60% versus 28%). However, all patients treated with postoperative radiation had developed local recurrences by 10 years. The authors concluded that postoperative radiation improved disease-free survival in patients with lumbosacral chordoma.²⁶⁸

The UCSF Lawrence Berkeley experience with charged-particle radiotherapy for chordoma was initially reported by Saunders *et al.*, and more recently by Schoenthaler *et al.*^{269,270} Fourteen patients with sacral chordomas were treated with neon or helium ion beam radiation at the Lawrence Berkeley laboratory. They received a median dose of 74.65 cGyE. The overall 5-year local control was 55%, with a mean follow-up of 65 months (range 22–164 months). Total resection, use of neon versus helium beams, and the absence of treatment breaks were associated with improved local control. Pain relief was achieved in all patients.²⁷⁰ More recently, Hug *et al.* published results of treatment for chordomas of the sacrum and spine (excluding base of skull) in 14 patients using combined photon and proton radiotherapy. Doses ranged between 67.1 and 82.0 cGyE (mean 74.6 cGyE). Nine of 14 (64%) were locally controlled. Local control was better for primary (90%) versus recurrent (50%) chordoma. There was a trend for improved local control for doses greater than 77 cGyE.¹¹⁶ Although chordomas are rare, several guidelines emerge from the literature. Chordomas are best treated with as complete a surgical resection as possible. Postoperative radiation can delay recurrence,

and palliate symptoms from unresectable disease. Palliation of pain can be obtained with doses of 40–50 Gy. Higher doses probably do not benefit patients with unresectable disease. However, in the postoperative setting, higher doses can be given safely with careful immobilization, MR/CT three-dimensional treatment planning and precision radiotherapy technique such as charged-particle, stereotaxic or intensity-modulated radiotherapy. Higher doses (>70 Gy) will maximize the durability of local control in the setting of a maximally resected tumor.

TREATMENT TECHNIQUES

Treatment Conference

Optimal radiotherapy for most soft-tissue sarcomas is a multidisciplinary effort requiring close cooperation between the surgeon, radiation oncologist, radiologist, pathologist, physical therapist and medical oncologist. A multidisciplinary treatment planning conference facilitates review of individual evaluation by each specialist, allows focused attention to specific details of the case (i.e. tumor histology, location, extent, operative findings, margin status) and allows the formulation of a consensus plan which addresses the medical, functional, cosmetic and psychosocial needs of the patient.

Radiotherapy Planning

Radiation Therapy Pre-Planning

An intimate knowledge of the anatomic structures involved by tumor is required to adequately plan the extent and configuration of the pre-resection target volume. Careful physical examination, and review of the tumor extent as depicted on staging radiographic studies with the soft-tissue radiologist and oncologic surgeon are required. Soft-tissue sarcomas usually remain confined to the muscular compartment or potential space of origin until they are very advanced, at which time multiple muscle compartment and/or anatomic structures (i.e. nerve, vessels, bone, visceral organs) can be involved. The original gross tumor volume (GTV) should be defined and carefully recorded for future comparison to treatment planning MR or CT scans.

Patient Positioning and Immobilization

One of the most critical steps in treatment planning is patient positioning and immobilization. This is done on the simulator table at the time of the initial set-up. The patient must be lying or seated comfortably to allow daily, reproducible immobilization which is as effortless

as possible. The lesion should be positioned such that the entrance and exit of the beam(s) do not expose contralateral limbs or other tissues unnecessarily. Once the treatment position has been chosen, immobilization devices such as plastic casts, foam vacuum casts, or thermoplastic molds are constructed to immobilize the region to be treated. Following this, the proximal and distal borders of the region of interest are demarcated on the patient and on orthogonal plain X-rays as a set-up reference. A treatment planning CT scan, and preferably a treatment planning MR, are obtained of the demarcated area immobilized in the treatment position. CT/MR image fusion is currently employed routinely at the National Cancer Institute for radiation treatment planning of soft-tissue sarcoma. An example of a CT/MR image fusion used to plan treatment of a pelvic Ewing's sarcoma is shown in [Figure 5.10](#).

Computer-assisted Treatment Planning

Many contemporary computer three-dimensional treatment planning systems allow CT/MR image fusion. This can be quite useful in ensuring accurate inclusion of areas of marrow involvement, and subtle periosteal soft-tissue edema resulting from tumor infiltration, within the target volume. The tumor is outlined or contoured on a slice-by-slice basis. Once this is complete, the gross tumor volume (GTV) has been defined. With the addition of appropriate margins (see below in preoperative/postoperative volumes), this volume becomes the clinical target volume (CTV). Sarcomas tend to be irregular tapering volumes within sloping body contours. Simple AP-PA fields are rarely optimal. Multiple matched coplanar oblique fields are often necessary to produce homogeneous doses in anatomic regions which taper in thickness and depth. Wedges, compensators, electron beams and carefully planned supplemental fields should be used to avoid areas of low or excess radiation dose. Shaped cerrobend blocks are being replaced by multileaf collimators which also allow the use of intensity-modulation techniques. An example of the technique used to treat a soft-tissue sarcoma of the posterior thigh is shown in [Figure 5.11](#).

Pre-operative Treatment Volume

Although it has been known for some time that sarcomas can extend along tissue planes for many centimeters,⁵⁶ and can recur more than several centimeters away from the tumor bed following resection and postoperative radiation, the required margin around the tumor has not been adequately studied prospectively in the preoperative setting. Radiotherapy volumes which treat <5 cm of normal tissue in the longitudinal

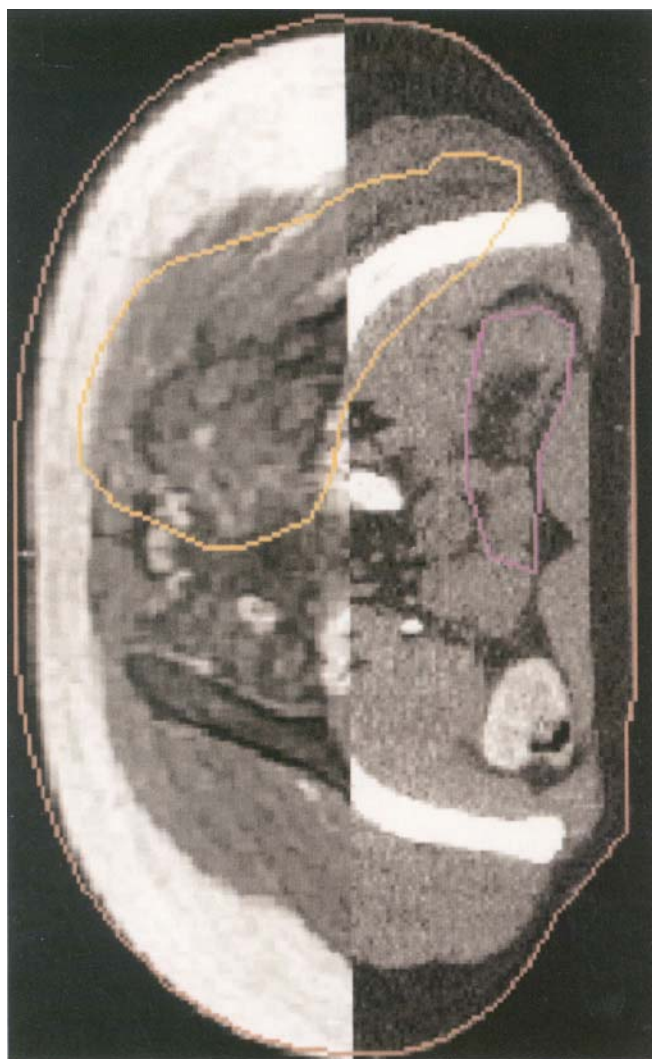


Figure 5.10 CT/MR image fusion used for treatment planning. The tumor and dose-limiting normal tissues are contoured on both CT and MR image sets and the composite contour is used for treatment planning.

dimension have been associated with an increased risk of recurrence in the postoperative setting.⁷ The preoperative CTV for tumors <10 cm in diameter should encompass the tumor with a longitudinal margin of at least 5 cm. For tumors >10 cm the CTV should include the tumor plus at least 7–10 cm longitudinal margin. Medirolateral margins for lesions in extremities can be limited to 2–3 cm where bone, interosseous membrane and facial planes define the boundary of an uninvolved compartment. Every attempt should be made to avoid circumferential radiation of an extremity to avoid development of edema due to complete obliteration of lymphatic egress. The minimum strip of soft tissue which should be spared is 2–3 cm; however, the more

soft tissue which is spared from the target volume, the better the potential functional outcome.

Preoperative Dose

If concurrent chemotherapy is not to be used, 50 Gy is given in 1.8–2.0 Gy fractions has been shown to be adequate. This is followed by resection 2–3 weeks later. In the setting of concurrent neoadjuvant chemotherapy 2.5–3.5 Gy fractions can be used to total doses of 28–35 Gy followed by resection 10–14 days later.

Postoperative Target Volume

In the postoperative setting the GTV consists of the tumor bed, the surgical field and any potential spaces which require drainage or which contain postoperative fluid collections (i.e. seroma or hematoma). The surgical incision and all drain sites are included in this volume, which is considerably larger than the GTV in the preoperative setting. For tumors that are 10 cm or less an additional longitudinal margin of at least 5 cm is recommended. This volume constitutes the postoperative CTV. For tumors >10 cm the CTV should include the GTV plus an additional 7–10 cm longitudinal margin. Bone, interosseous membrane and intact fascia restrict the medirolateral extension of sarcoma such that medirolateral margins need not be greater than 3 cm. The surgical incision and all drain sites should be treated, and bolus should be used if necessary to eliminate skin-sparing at these sites due to nontangential exposure. Circumferential radiation of an extremity should be avoided if at all possible. Preferably one-third of the width of a limb should be spared, but whenever possible not less than 2–3 cm, in order to prevent severe extremity lymphedema.

Postoperative Dose

In the postoperative setting of negative margins a total dose of 63 Gy is routinely used at the NCI. The initial CTV is treated to 45 Gy. Subsequently the CTV is decreased to 2 cm beyond the GTV, and this second CTV is used to deliver the final 18 Gy for a total dose of 63 Gy. Daily fraction sizes of 1.8–2.0 Gy are used. It is recommended by some authors to decrease the total dose by 10% if concurrent chemotherapy is given. This has never been the policy at the NCI. If margins are microscopically positive the total dose should be increased to 66–70 Gy utilizing a CTV which is limited to the region of margin positivity plus 2 cm. For patients with gross tumor which is to be treated curatively with radiation alone, the total dose should be 72–76 Gy. In this setting a “shrinking-field” technique should be

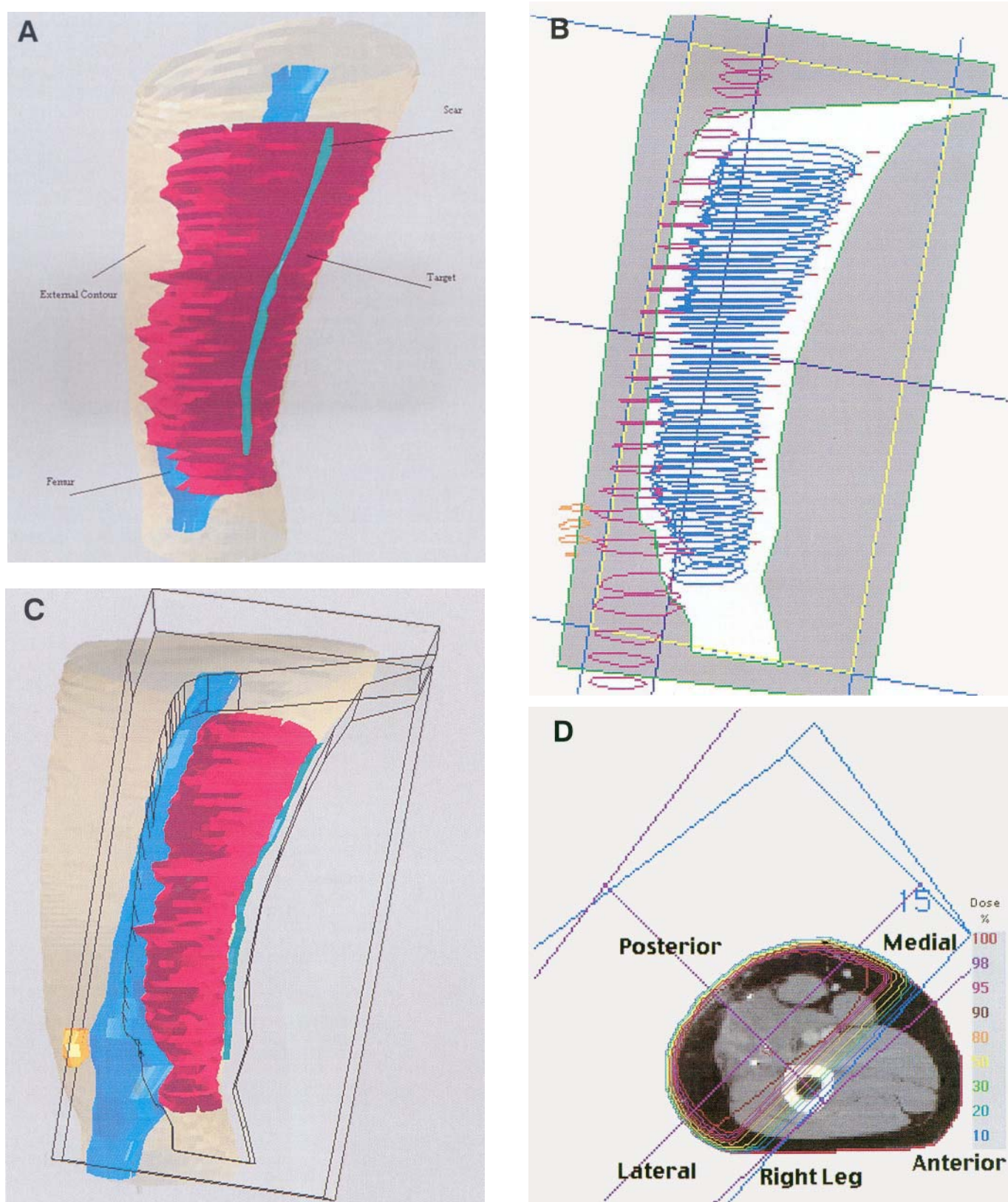


Figure 5.11 Three-dimensional treatment planning for a thigh sarcoma. In (A) a three-dimensional posterior/oblique projection displays the clinical target volume, the incision scar, the femur, and the external contour of the thigh. (B) and (C) show a beam's eye view of the target volume and computer-generated shaped blocks. Wire diagrams of the CT/MR contours (the block is shaded gray) are shown in (B) and three-dimensional surface contours are shown in (C). A cross-section showing the dose distribution through the tumor at the isocenter is shown in (D).

used. This consists of multiple consecutively smaller CTVs culminating in a volume which encompasses gross tumor with 1.0 cm margin.

Hands and Feet

Treatment of hands and feet requires special consideration if a good functional outcome is to result.

Hand

Sarcomas arising on the hand and wrist should be treated with the hand outstretched and flattened on a board; one is shown in [Figure 5.12](#). An immobilization cast should be fabricated to ensure precise daily repositioning of the treated limb. Because tumors arising in the hand tend to be relatively small when diagnosed, and due to the limited volume of the hand, the normal margin guidelines for truncal and extremity sites do not necessarily apply. For resected lesions on the hand the CTV should include the surgical tumor bed, which should be demarcated by clips placed at the time of surgery plus 2 cm medially and laterally, and 4–6 cm longitudinally. The incision and any drain sites should be treated with bolus if necessary, to ensure that they receive full dose per fraction. Care must be taken to avoid treatment of the nailbeds and distal interphalangeal joints if possible. Sparing as much of the palmar aponeurosis as possible will help prevent the development of a flexion contracture. Circumferential treatment of the hand and fingers should be avoided, to prevent edema and contracture. If one limb of the arterial arcade of the hand can be spared, this may help reduce late soft-tissue and muscle atrophy. Arteriograms of the hand and wrist in the immobilized treatment position may be helpful in this regard. Treatment beams are usually parallel opposed in the dorsal/plantar direction. An example of the treatment technique used for a hand is shown in [Figure 5.13](#).

Feet

The steeply sloping and irregular contours of the foot, and its relatively small size, pose a unique challenge with respect to achievement of a homogeneous dose distribution. Custom immobilization devices, complex compensators and sophisticated treatment planning

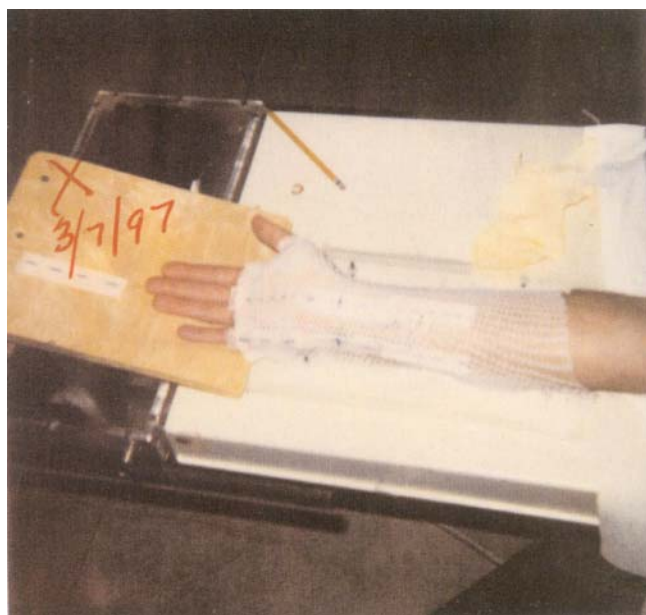


Figure 5.12 An immobilization device used for treatment of a hand sarcoma. The hand is in an outstretched and flat position to allow treatment with opposed anterior and posterior beams.

should be routinely employed. Immersion of the foot in a waterbath is a technique which has been employed to achieve a homogeneous electron equilibrium within the target volume in the foot, which may vary considerably in tissue thickness. Lesions on the proximal portion of the foot are treated with beams which enter and exit over the lateral and medial surfaces. Lesions on the more distal aspect of the foot are treated with beams entering and exiting over the dorsal/ventral surfaces. Careful attention is paid to avoidance of treating the entire width of the plantar aponeurosis, otherwise a resulting flexion contracture could lead to a useless, painful, clubbed foot and ultimately a palliative amputation. Whenever possible the Achilles tendon, the heel, the sole, the toes and the nailbeds should be spared as long as treatment of the tumor or its bed will not be compromised. Electron beams can be useful in boosting scars, and in preventing full-thickness radiation if this is not desired. Bolus should be used over scars to ensure full dose unless high-energy electrons or tangential beams eliminate skin-sparing.

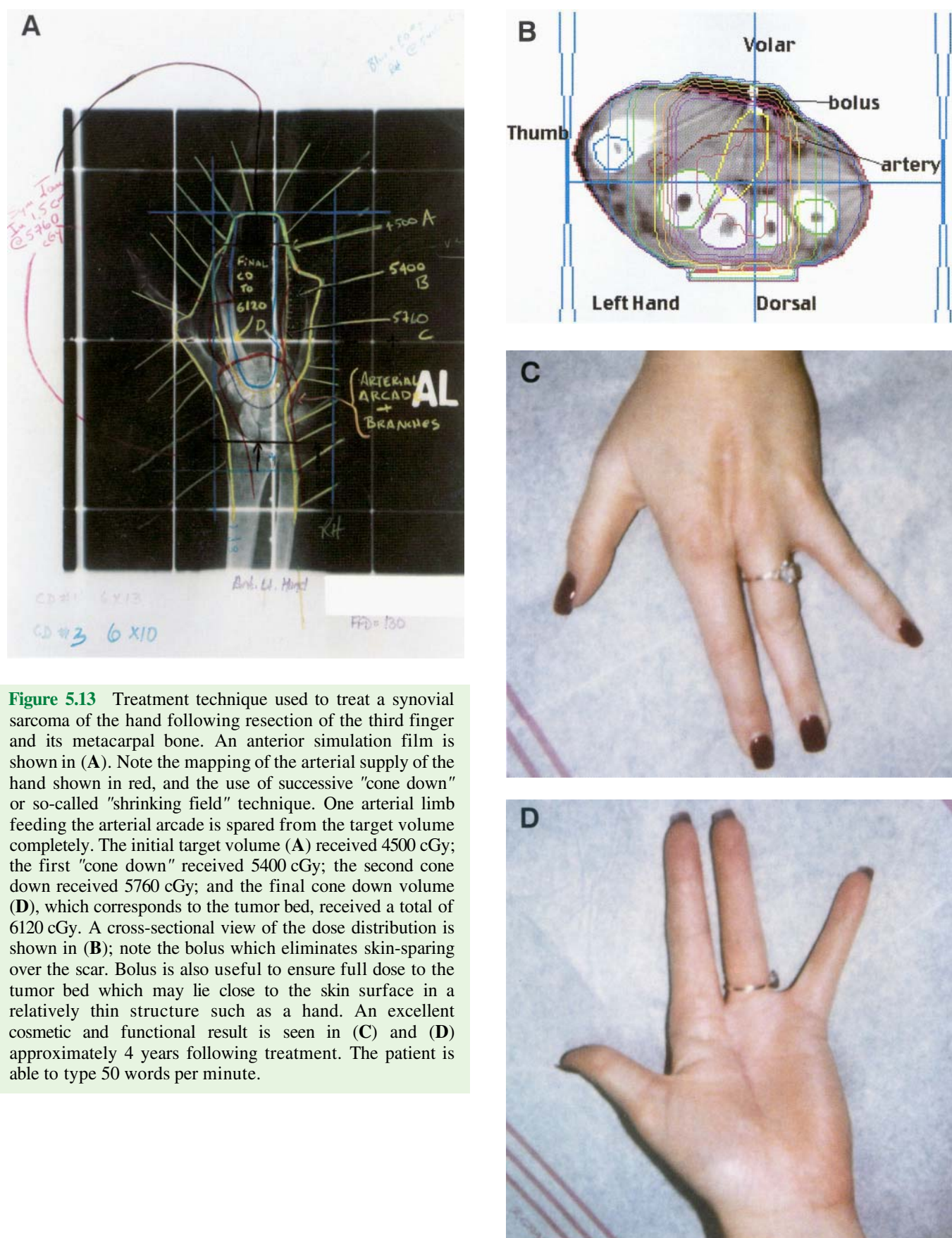


Figure 5.13 Treatment technique used to treat a synovial sarcoma of the hand following resection of the third finger and its metacarpal bone. An anterior simulation film is shown in (A). Note the mapping of the arterial supply of the hand shown in red, and the use of successive "cone down" or so-called "shrinking field" technique. One arterial limb feeding the arterial arcade is spared from the target volume completely. The initial target volume (A) received 4500 cGy; the first "cone down" received 5400 cGy; the second cone down received 5760 cGy; and the final cone down volume (D), which corresponds to the tumor bed, received a total of 6120 cGy. A cross-sectional view of the dose distribution is shown in (B); note the bolus which eliminates skin-sparing over the scar. Bolus is also useful to ensure full dose to the tumor bed which may lie close to the skin surface in a relatively thin structure such as a hand. An excellent cosmetic and functional result is seen in (C) and (D) approximately 4 years following treatment. The patient is able to type 50 words per minute.

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6

The Biology and Role of Cryosurgery in the Treatment of Bone Tumors

Jacob Bickels, Isaac Meller and Martin Malawer

OVERVIEW

The application of liquid nitrogen as a local adjuvant to curettage in the treatment of bone tumors was first introduced three decades ago. This technique, termed cryosurgery, was shown to achieve excellent local control in a variety of benign-aggressive and malignant bone tumors. However, early reports showed that cryosurgery has been associated with a significant injury to the adjacent rim of bone and soft tissue, resulting in high rates of fractures and infections. These results reflected an initial failure to appreciate the potentially destructive effects of liquid nitrogen and establish appropriate guidelines for its use. This chapter reviews the biological effect of cryosurgery on bone, surgical technique, and current indications for its use.

INTRODUCTION

Cryosurgery is the therapeutic use of cold to induce tissue necrosis with ablative intent. The first report of the use of local freezing as a treatment modality is attributed to Dr. James Arnott, who described in 1850 the direct application of a salt-ice mixture to various skin lesions.¹ He noticed a marked anesthetic and hemostatic effect and advocated its use, mostly as a palliative treatment, in a large variety of diseases, ranging from headache to advanced carcinoma of the cervix and fungating breast cancer. For almost a century, cryosurgery was practiced by a handful of surgeons in the fields of neurosurgery, gynecology, urology, and ophthalmology. Solid carbon dioxide, cold air blast, and liquid nitrogen (LN) were used as cryogenic agents in the treatment of various benign and malignant lesions and achieved good results in terms of local tumor control and residual scarring.²

In 1962 Cooper described a cryotherapy unit in which LN was circulated through a hollow metal probe.³ This equipment made it possible, by means of interrupting the flow of liquid nitrogen, to control the temperature of the tip of the probe within the range of room temperature to -196°C . Because this was a totally closed system, one could apply the cold to any point in the body accessible to the probe. The first clinical application of this technique, termed a "closed system", was in the treatment of Parkinson's disease.² Gage *et al.* treated malignant soft-tissue lesions of the oral cavity with cryotherapy and observed that the adjacent frozen bone eventually healed.⁴ In their classic study Gage *et al.* used a closed system of latex tubes with LN circulating within coils surrounding the diaphyses of dog femora.⁴ LN was used as a cryogenic agent because of its capability to induce rapid freezing of large lesions. The procedure was demonstrated to induce bone necrosis, followed by slow healing and new bone formation.⁴⁻⁶

The first use of cryosurgery in conjunction with orthopedic surgery is attributed to Marcove and Miller, who described an "open system" technique that entailed pouring LN directly into a tumor cavity.⁷ They treated a 48-year-old male with a painful metastatic lung carcinoma to the proximal humerus that was resistant to radiation therapy. The patient experienced complete relief of his pain following treatment.⁷ Liquid nitrogen was shown to achieve local tumor control with minimal bone and functional loss, and cryosurgery was soon practiced in conjunction with surgery for a large variety of bone tumors.⁷⁻¹⁰

Despite its demonstrated benefits, LN is a powerful local adjuvant that, when not used with caution, may cause significant injury to the adjacent rim of bone,

cartilage, and soft tissues and result in secondary fracture, skin necrosis, infection, and temporary neuropraxia.^{7,8,11} The early series had high complication rates that reflected an initial failure to appreciate these potentially destructive effects and establish an appropriate surgical technique. This high complication rate gave this modality a poor reputation, and during the past three decades only a few orthopedic surgeons used cryosurgery routinely. Nonetheless, their experience helped to define the precautions and indication for its use. Cryosurgery was found to be effective in the treatment of liver metastases^{12,13} and genitourinary malignancies.¹⁴⁻¹⁶ In the field of orthopedic oncology, cryosurgery was shown to be a curative procedure in treatment of benign-aggressive and low-grade malignant bone tumors. Cryosurgery could also achieve local tumor control and symptomatic relief in metastatic bone disease.¹⁷⁻²³ This chapter reviews the biological effect of cryosurgery on bone, its advantages and limitations, surgical technique, and current indications for its use.

BIOLOGY OF CRYOSURGERY

Liquid nitrogen, stored at -196°C , is an effective cryogenic agent that can be used for either tissue preservation or destruction. A slow freeze and quick thaw allow tissue preservation; a quick freeze and slow thaw lead to its destruction.²⁴ Cryosurgery utilizing LN is effective in the treatment of bone tumors because bone necrosis occurs at temperatures below -21°C .^{4,25} The formation of intracellular ice crystals and membrane disruption are considered the main mechanisms of LN-induced cellular necrosis. Other mechanisms of cytotoxicity include electrolyte changes, denaturation of cellular proteins, and microvascular failure.²⁶⁻³¹ During cryotherapy the rapid freeze causes intracellular ice crystals to form. As the temperature rises during thawing, these crystals coalesce and mechanically disrupt the cell membrane, causing cell death. Repetitive freeze-thaw cycles increase the amount of necrosis. These changes are explained by increased thermal conductivity within the frozen lesion that results from an alteration in the basic structure of the tissue and are proportional to the time of exposure to LN.^{4,24}

Histological evaluation of the cortex, immediately following cryosurgery, shows minimal changes. The extent of cortical injury does not become evident until a week after application of LN; by this time, periosteum over the previously frozen cortex has disappeared, and the denuded bone appears dull white. The most dramatic effect of LN application may be seen in the bone marrow and is characterized by extensive necrosis with minimal inflammation and subsequent liquefaction with progressive fibrosis. Large, thickened

thrombosed vessels are occasionally seen.^{4–6,28} Bone repair, beginning in the periphery of the bone cavity, occurs slowly and is first evident at the seventh to eighth week. Only after 5–6 months is the new bone formation sufficient to prevent pathologic fracture. The histological features after repeated freeze–thaw cycles are almost identical to those described for a single episode of freezing.⁴

Malawer *et al.* demonstrated a 7–12-mm rim of bone necrosis with no effect on articular cartilage when liquid nitrogen was utilized in a dog model (Figure 6.1).²⁸ Marcove *et al.* stated that three freeze–thaw cycles produce tumor cell death up to 2 cm from the cavity margin.¹⁰ This extent of bone destruction makes cryosurgery, which is by definition an intralesional surgical modality, as effective as a wide resection in the treatment of benign-aggressive, low-grade primary bone sarcomas, or metastatic lesions.^{8,9,17,22} High-grade bone sarcomas, on the other hand, usually have a significant soft-tissue extension that is not affected by LN, unless poured directly on it. This is not recommended due to the expected damage to the surrounding muscles and neurovascular bundle. Articular cartilage seems to be resistant to cryotherapy and remains intact, even when freezing extends to the subchondral bone or crosses the joint.^{17,32}

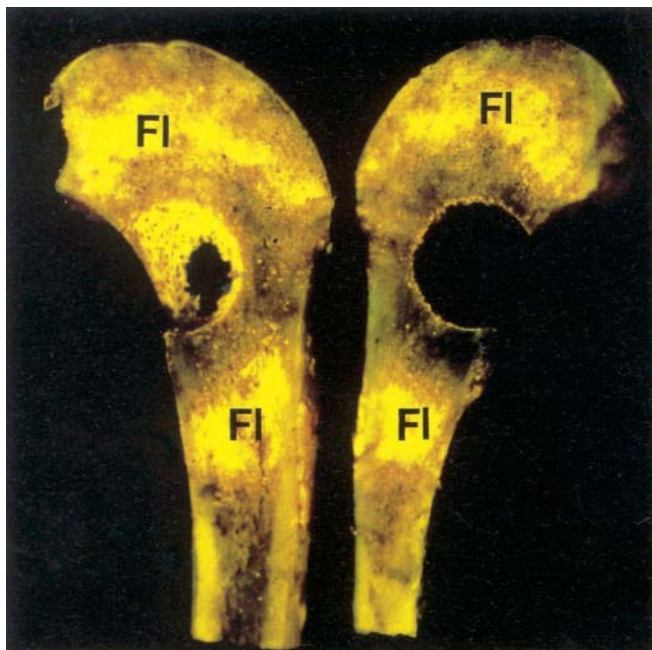


Figure 6.1 Tetracycline fluorescence of a dog femora following cryosurgery demonstrates a circumferential rim of no fluorescence around the cavity, which is the result of bone necrosis. The outer rim of fluorescence (FI) corresponds to attempted bony repair in the adjacent viable tissue. (Acta Orthop Scand 1999;70(3):308–315)

SURGICAL TECHNIQUE

Although a simple procedure, cryosurgery can cause significant morbidity if performed inappropriately. An effective and safe procedure must follow these consecutive steps: (1) adequate exposure of the tumor cavity; (2) meticulous curettage and burr drilling; (3) soft-tissue mobilization and protection prior to introduction of LN to the tumor cavity; (4) internal fixation of the cavity after cryotherapy; and (5) protection of the operated bone throughout the healing period.

Exposure

When possible, a pneumatic tourniquet is used during the procedure to decrease local bleeding and prevent blood from acting as a heat sink and a thermal barrier for the cryotherapy. Benign-aggressive, low-grade primary bone sarcomas, and metastatic tumors, rarely invade the articular cartilage, and an extracapsular approach is therefore possible in most cases. Violation of the joint cavity must be avoided because of the possibility that it may be contaminated by tumor cells and the risk of injury to the cartilage following direct exposure to LN. After exposure of the involved bone and soft tissues, a cortical window the size of the longest longitudinal dimension of the tumor is made. To minimize additional bone loss the tumor is approached through the retained thinned or destroyed cortex. A large cortical window is essential to expose the entire tumor and avoid inadequate curettage. The window must be elliptical, and its axis must be parallel to the long axis of bone in order to reduce the stress rising effect (Figure 6.2).

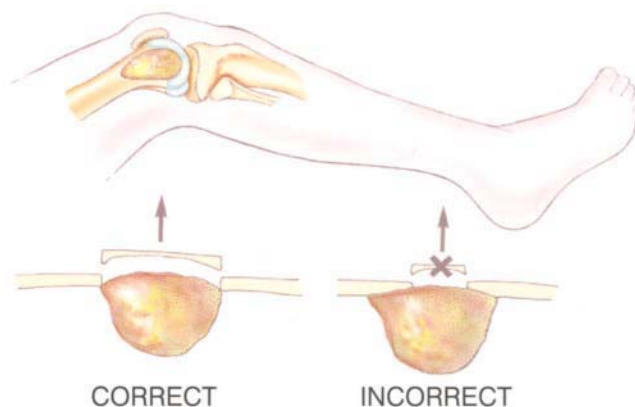


Figure 6.2 A large cortical window, the size of the largest diameter of the lesion, is essential for adequate exposure. A smaller window is not sufficient for complete curettage and burr drilling of the tumor. (Acta Orthop Scand 1999;70(3):308–315)

Curettage

All gross tumor is removed with hand curettes. After the neoplastic tissue is curetted away from the inner wall of the lesion the reactive wall reveals an irregular contour. This irregularity makes it virtually impossible to remove all the tissue from the inner reactive shell with a curette. Therefore, curettage is followed by high-speed burr drilling with Midas Rex® (Midas Rex, Forth Worth, TX) or Black Max® (Anspach, Lake Park, FL; Figures 6.3, 6.4).

Cryosurgery

Before introduction of the LN, bony perforations are identified and sealed, and the surrounding skin, soft tissues, and neurovascular bundle are protected by mobilization and shielding with Gelfoam® (Upjohn, Kalamazoo, MI). Large skin flaps are retracted to protect them from possible spillage of the LN.

Liquid nitrogen can be applied to a bony cavity by direct pour (open system) or by perfusing it through metal probes (closed system).^{2,3,33} Cryosurgery is not effective unless a close contact is achieved between the LN and the outermost layer of the tumor cavity. Therefore, size and configuration of the tumoral cavity are determinators of the chosen technique. Most bone lesions have a large, irregular inner wall, and use of the open system makes it possible to homogeneously spread the LN throughout the cavity. Liquid nitrogen spray is an "open system" modality, used for unique anatomic locations in which pouring of LN is not technically feasible (for example, deep-seated pelvic lesions). The closed system, on the other hand, can be effectively used in small, regular cavities, such as those remaining after curettage of a small lesion in the digits or the distal radius.

Using the open system, LN is poured through a stainless-steel funnel into the tumor cavity. Care is

taken to fill the entire cavity. The Gelfoam® blocks immediately freeze, forming a tight seal around the funnel. Thermocouples are used to monitor the freezing effect within the cavity, cavity wall, and adjacent soft tissue, as well as the rim of bone 1–2 cm from the periphery of the cavity. The surrounding soft tissues are continuously irrigated with warm saline solution to decrease the possibility of thermal injury (Figures 6.5–6.8). In each cycle, LN is left in the cavity until it has completely evaporated. Each cycle lasts 1–2 min and is proportional to the volume of poured LN. Spontaneous thaw is then allowed to occur over a period of 3–5 min. Once the temperature of the cavity rises above 0°C the cycle is considered complete. Two freeze–thaw cycles are administered, at the end of each of which the cavity is irrigated with saline solution.

Reconstruction

Reconstruction is performed using polymethyl-methacrylate (PMMA), internal fixation, and subchondral bone graft. The subchondral surface is reconstructed with bone graft prior to cementation (Figures 6.9–6.15). Internal fixation is strongly recommended, as indicated by recently reported long-term follow-up results in a large series of patients with giant-cell tumor of bone who were treated with cryosurgery.¹⁷ In that series, fractures occurred only when internal fixation was not used as part of reconstruction. The combination of PMMA and internal fixation provides immediate stability and structural support for large defects and allows early rehabilitation of the adjacent joint.

Postoperative Management

Routine perioperative prophylactic antibiotics are administered for 3–5 days. The wound is examined on

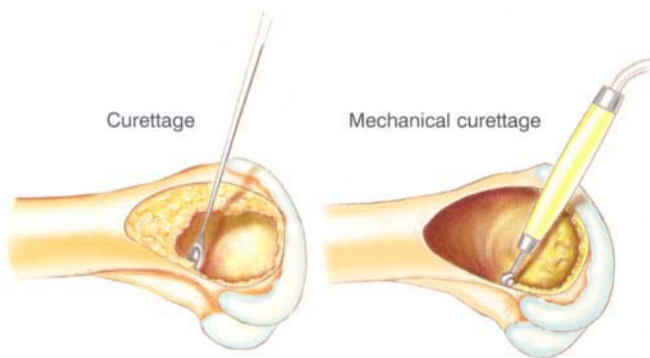


Figure 6.3 Curettage of the tumor cavity is followed by meticulous burr drilling until normal bone is seen circumferentially. (Acta Orthop Scand 1999;70(3):308–315)

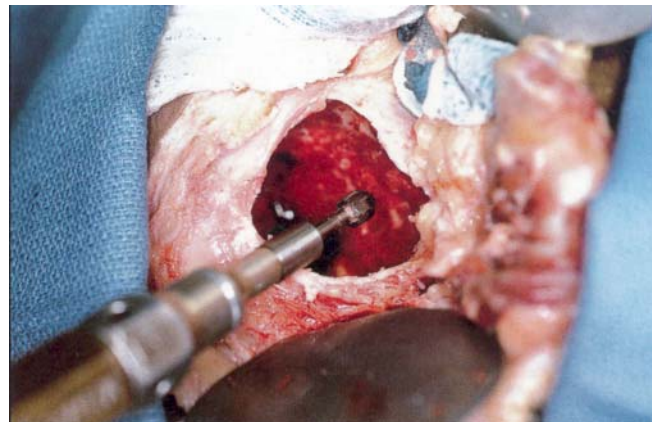


Figure 6.4 Burr drilling of a tumor cavity using the Midas Rex® system (Midas Rex, Forth Worth, TX).



Figure 6.5 Liquid nitrogen is poured through a stainless-steel funnel. Temperature within the cavity, as well as in the surrounding bone and soft tissues, is monitored with thermocouples. Soft tissues are protected with Gelfoam® and irrigated continuously with warm saline solution.



Figure 6.6 Cryosurgery of the proximal phalanx of the fourth finger.



Figure 6.7 Cryosurgery of the proximal phalanx of the third toe. Mobilization and protection of the soft tissues is practiced in all anatomic locations.

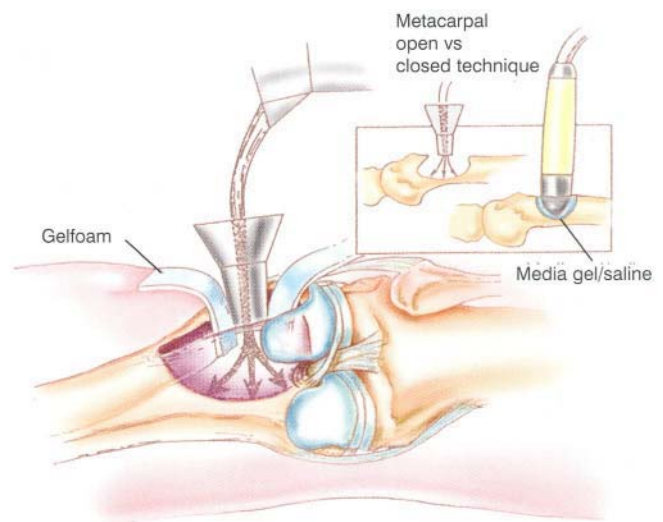


Figure 6.8 Illustration of the direct pour (open system) technique of cryosurgery. (*Acta Orthop Scand* 1999;70(3):308–315)

the third day after surgery. If the skin is intact, passive and active motion of the adjacent joint are performed. Patients with lesions of the lower extremities are kept partial-weight-bearing for 6 weeks. Plain radiography is then performed to rule out fracture and establish bone graft incorporation. If healing is progressing satisfactorily, weight-bearing is allowed. Patients are instructed to avoid high-impact activities for 6 additional months.

Complications

The exposure of normal bone and soft tissues (skin, muscles, nerves, and blood vessels) to the freezing effect

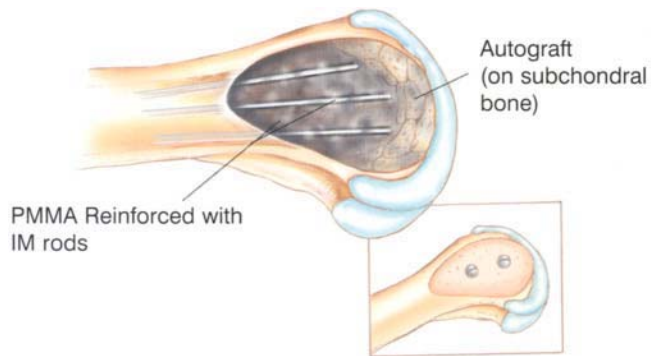


Figure 6.9 Reconstruction of the tumor cavity, using subchondral bone graft, followed by intramedullary hardware and polymethylmethacrylate. That type of composite reconstruction is used in all anatomic locations. (*Acta Orthop Scand* 1999;70(3):308–315)

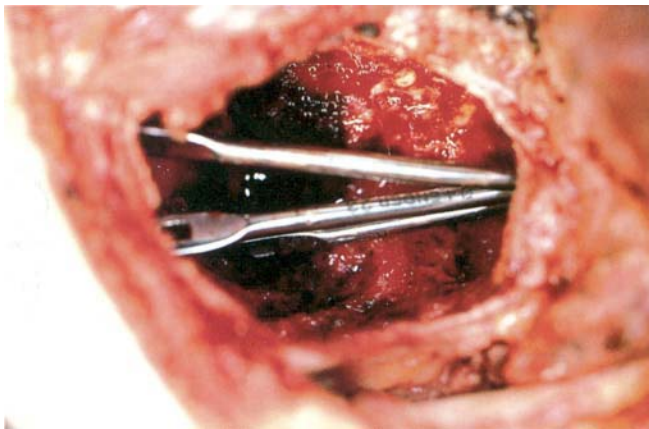


Figure 6.10 Reconstruction of the proximal tibial metaphysis with Ender rods.

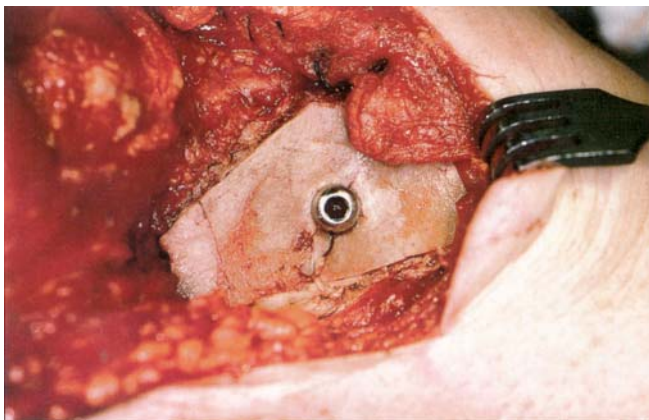


Figure 6.11 Following cementation, the cortical window is covered with autologous corticocancellous iliac bone graft.

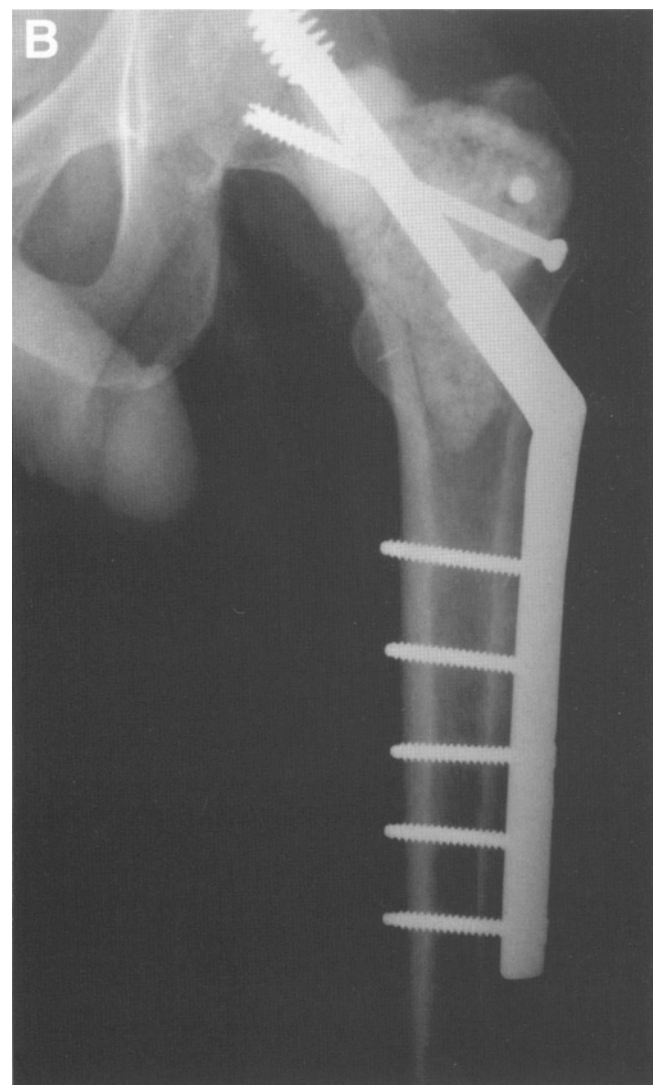


Figure 6.12 (A) Giant-cell tumor of the proximal femur (marked with arrows) in a 31-year-old patient. (B) Following cryosurgery the tumor cavity was reconstructed with subchondral bone graft, PMMA, and supported with a side plate, sliding nail, and a screw. The cortical window was covered with a corticocancellous bone graft.

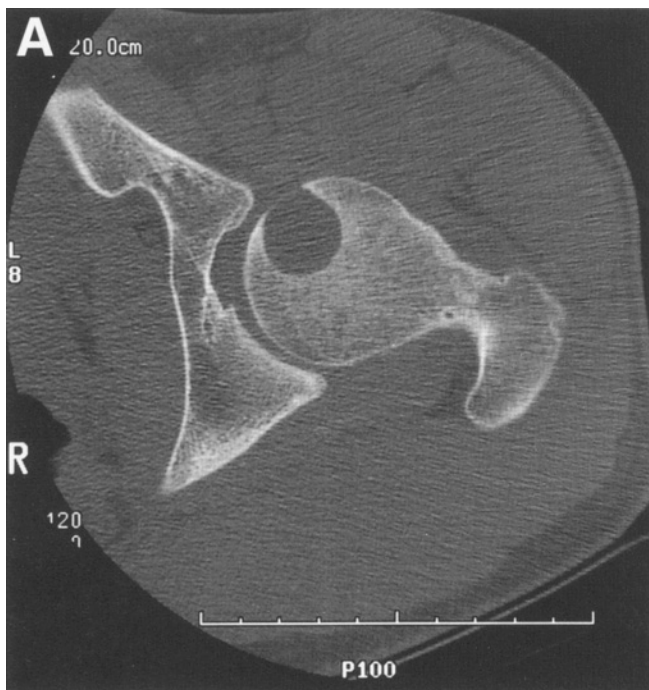


Figure 6.13 (A) Computed tomography of the femoral head of a 19-year-old patient, showing a chondroblastoma. Due to its anterior location the femoral head and neck were exposed using the Watson–Jones approach without dislocation of the femur. Curettage, burr drilling, and cryosurgery were performed. (B) These were followed by autologous iliac bone graft, reinforcement with PMMA, and internal screw fixation.



Figure 6.14 Cryosurgery of the talus for a giant-cell tumor of bone. Tumor cavity was reconstructed with subchondral bone graft, PMMA, and internal fixation.



Figure 6.15 Cryosurgery of the first metatarsal for a giant-cell tumor of bone. Tumor cavity was reconstructed with subchondral bone graft, PMMA, and internal fixation.

of LN can result in significant morbidity. Early studies of the use of cryosurgery in the treatment of bone tumors reported high complication rates, mostly pathological fractures and infection (Table 6.1). Many of these early investigators did not recognize the importance of soft-tissue protection, use of PMMA and internal fixation for reconstruction, and avoidance of significant impact on the operated extremity until healing was complete. Gage *et al.* performed cryosurgery on 34 dog femora and documented a 32.3% pathologic fracture rate when activity was not restricted and the operated bone was not protected.⁴ Marcove *et al.* practiced cryosurgery prior to the use of PMMA combined with onlay bone graft and/or internal fixation.¹⁰ They made only a minimal attempt to reconstruct the bone defect remaining after curettage and cryosurgery and reported a postoperative fracture rate of 25% in the early series (Figure 6.16). Malawer *et al.* reported a 5.9% rate of pathologic fractures following cryosurgery among 102 patients, treated with cryosurgery for giant-cell tumor of bone.¹⁷ As mentioned, all these fractures occurred when internal fixation was not used for reconstruction.

Prophylactic antibiotics, wide exposure, and adequate mobilization of skin flaps and adjacent neurovascular bundle, along with continuous irrigation of tissues with warm saline solution, reduce the incidence of skin necrosis. Malawer *et al.*, who used this technique, reported no cases of infection and only three cases (2.9%) of partial skin necrosis.¹⁷ The latter were the result of contact with leaking LN and were satisfactorily managed with nonsurgical treatment. Nerve palsy after exposure to LN occurs in less than 1% of patients and is usually transient.^{17,20,33}

CLINICAL APPLICATION

Table 6.2 summarizes the reported series on bone tumors treated with cryosurgery. The most extensive orthopedic surgical experience with cryosurgery, by far, has involved giant-cell tumor (GCT) of bone, a benign-aggressive primary bone tumor. Seventy percent of these lesions occur in the third or fourth decades of life, and in most cases they are located in the metaphyseal–epiphyseal region of long bones.³⁴ Because wide excision of these tumors would cause significant functional limitation, due to their proximity to the joint, intralesional procedures have been common practice; however, the rate of local recurrence, mainly after curettage, has been unacceptably high (i.e. 40–55%).^{35–38} The introduction of LN as an adjuvant to meticulous curettage and burr drilling significantly lowered the recurrence rate; Malawer *et al.* used cryosurgery in the treatment of GCT of bone and reported a 2.3% recurrence rate among patients treated primarily with cryosurgery.¹⁷

Marcove and Miller used cryosurgery to treat a variety of benign and malignant bone tumors and concluded that it should be reserved for benign-aggressive bone tumors.⁷ Surgical treatment of high-grade primary bone sarcoma necessitates wide excision of the tumor with its soft-tissue component; any violation of the tumor margins is associated with a high risk of local tumor recurrence.³⁹ Cryosurgery is not an appropriate surgical modality for high-grade primary bone sarcomas for its being an intraosseous procedure with minimal effect on the soft-tissue component of the tumor. Bone tumors that have minimal or no soft-tissue component, such as low-grade, unicompartmental

Table 6.1 Summary of literature review on complication rates following cryosurgery

Author/year	Cases	Complications					
		Fracture	Infection	Skin necrosis	Join degeneration	Nerve palsy	Other
Marcove 1969	57	4	–	6	–	–	–
Marcove 1973	52	13	8	–	2	4	–
Marcove 1977	18	7	–	–	3	4	–
Jacobs 1985	12	6	–	–	–	–	–
Malawer 1991	25	2	–	1	–	–	Synovial fistula (1)
Aboulafia 1994	9	–	–	–	–	–	–
Marcove 1994	7	–	2	–	–	–	Rectal fistula (1)
Marcove 1995	51	5	–	–	–	1	–
Schreuder 1997	26	1	2	–	–	1	–
Schreuder 1998	26	2	1	–	–	–	Venous gas embolism
Malawer 1999	102	6	–	3	2	1	–

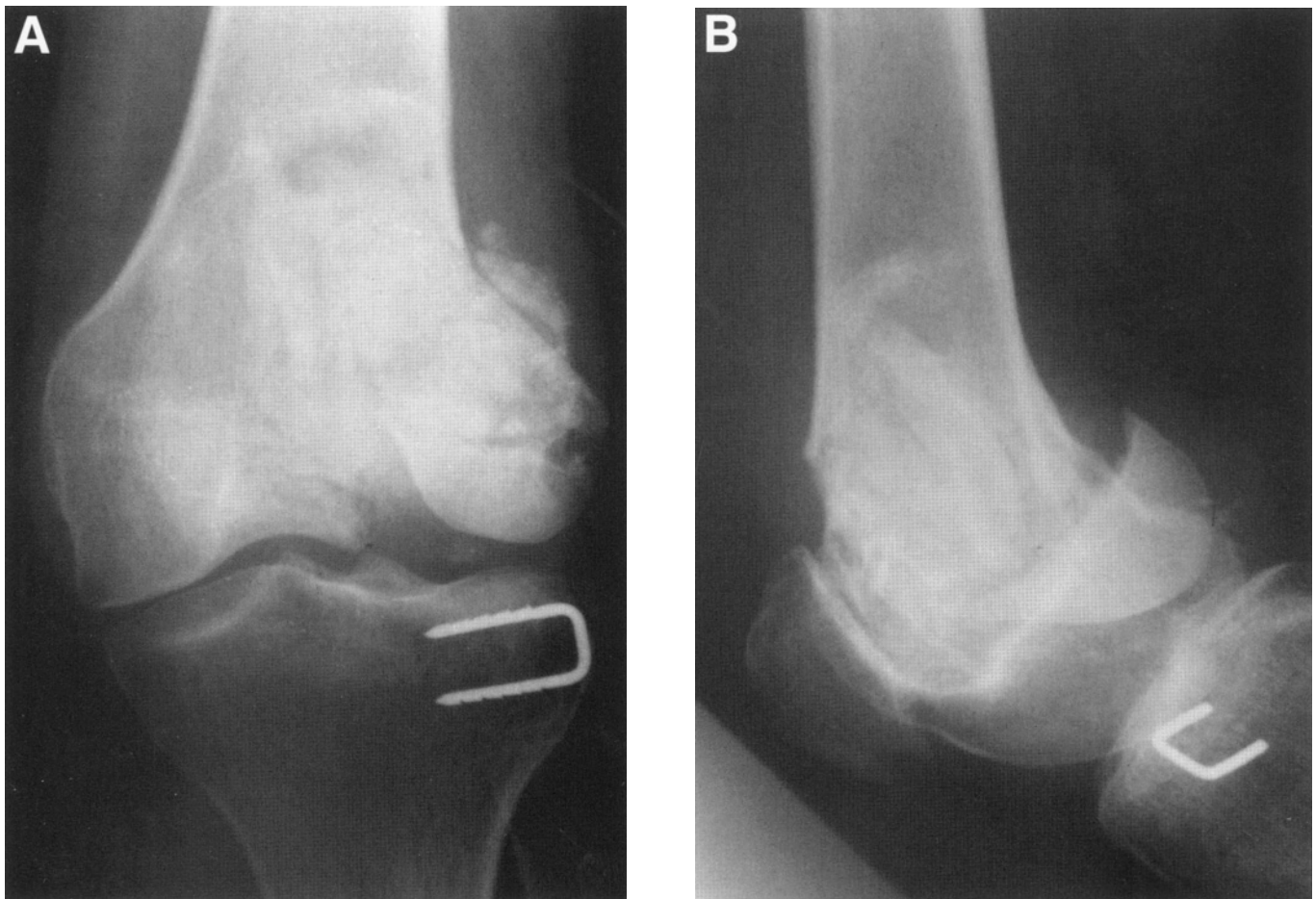


Figure 6.16 Plain radiographs of the distal femur: (A) anteroposterior, and (B) lateral views, showing a pathologic fracture of the lateral femoral condyle. The fracture occurred 18 months following cryosurgery, in which internal fixation was not used for reconstruction. Reinforcement of the tumor cavity with PMMA and internal fixation is strongly recommended in all cases.

chondrosarcomas and metastatic tumors of bone, can be treated with cryosurgery.^{7,9,22}

SUMMARY

Cryosurgery is an effective adjuvant to curettage for a variety of benign and malignant bone tumors. It is a curative procedure in the treatment of benign-

aggressive bone lesions as well as of low-grade primary bone sarcomas, and can achieve local control in metastatic bone disease. The previously reported high rates of fracture and infection can be avoided by careful attention to surgical details. Adequate exposure, meticulous curettage and burr drilling, soft-tissue mobilization and protection, and routine use of internal fixation with PMMA for reconstruction are essential.

Table 6.2 Summary of literature review on bone tumors treated with cryosurgery

<i>Tumor type</i>	<i>Author/year</i>
<i>Benign-aggressive lesions</i>	
Giant-cell tumor	Aboulafia 1994; Jacobs 1985; Malawer 1991, 1999; Marcove 1969, 1973, 1978, 1994
Enchondroma	Schreuder 1998
Chondroblastoma	Schreuder 1998
Unicameral bone cyst	Schreuder 1997
Aneurysmal bone cyst	Marcove 1969, 1995; Oeseburg, 1978; Schreuder 1997
Fibrous dysplasia	Marcove 1969
Hemangioma of bone	Marcove 1969
Sacral chordoma	Marcove 1969; Vries 1986
Eosinophilic granuloma	Marcove 1969
<i>Metastatic lesions</i>	
Carcinoma of lung	Marcove 1969
Carcinoma of breast	Marcove 1969
Carcinoma of prostate	Marcove 1969
Hypernephroma	Marcove 1969, 1977
Carcinoma of bladder	Marcove 1969
Soft-tissue sarcoma	Marcove 1969
Adenocarcinoma of uterus	Marcove 1969
<i>Primary bone sarcomas</i>	
Osteosarcoma	Marcove 1969, 1984
Chondrosarcoma	Marcove 1969; Marcove 1977, Schreuder 1998
<i>Other</i>	
Multiple myeloma	Marcove 1969

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7

Management of Abdominopelvic Sarcoma

Paul Sugarbaker

OVERVIEW

The principles of management of all sarcomas that involve the abdominal and pelvic cavity are presented. The anatomic sites for the primary malignancy include retroperitoneal sarcomas, pelvic side wall sarcomas, sarcomas arising from the abdominal viscera and sarcomas arising from the pelvic organs. All histologic types of sarcomas may be considered together when therapeutic options are being discussed. This presentation stresses surgical removal with an adequate margin of resection as the principal goal of management. The curative treatment of these cancers places great emphasis on the surgeon's knowledge of anatomy, technical skills, innovation and surgical courage. Systemic chemotherapy and radiotherapy have not shown reproducible efficacy. Complete clearance at the margins of resection and complete containment of tumor spillage remains the only reliable treatment option. Possible benefits of induction chemotherapy to reduce the size of advanced primary tumors prior to attempts at resection and intraperitoneal chemotherapy using heated cisplatin and doxorubicin for eradication of microscopic residual disease in the perioperative period are presented.

INTRODUCTION

Sarcomas are unusual but not rare malignancies. They account for only 1% of adult solid tumors. These sarcomas appear most frequently between the fourth and sixth decades of life with a 2:1 male/female ratio. They can arise anywhere in the body with the lower extremity being the most common site. Incidences are as follows: lower extremities (46%), upper extremities (13%), retroperitoneum, pelvis and visceral (12%), truncal sarcomas (19%), and head and neck sarcomas (9%)¹ (Table 7.1). The presenting symptoms and signs of all sarcomas are nonspecific. With sarcomas involving the abdominal and pelvic cavity diagnosis is even more subtle because these tumors may progress for long time periods without causing overt symptoms.¹ Further confusion may arise when abdominal and pelvic sarcomas mimic the more common types of gastrointestinal malignancy. However, complete cancer resection of even large abdominal and pelvic sarcomas can be associated with long-term survival and even cure.

In the past decade treatment results with extremity soft-tissue sarcomas have improved dramatically. Both survival and quality-of-life benefits have occurred as a result of new treatment approaches based on multimodality treatment. Recently, patients with sarcomas that involve the abdominal or pelvic cavity have experienced improvements in therapy. Modern treatments require an aggressive pursuit of a multimodality approach involving meticulous surgery and regional chemotherapy. Further studies with innovative treatment options are required to achieve a better outcome with these malignancies.

The purpose of this chapter is to critically review the results of management of sarcomas that involve the abdominal and pelvic cavity and to make recommendations regarding current strategies for management.

NATURAL HISTORY

Retroperitoneal and Pelvic Sidewall Sarcomas versus Visceral Sarcomas

The natural history of retroperitoneal and pelvic sidewall sarcomas differs significantly from the more common abdominal and pelvic adenocarcinomas and from visceral sarcoma. These variations are important when planning treatment. A unique feature of many retroperitoneal and pelvic sidewall sarcomas concerns their large size at the time of diagnosis.¹⁻⁴ These fleshy tumors often push rather than invade into the surrounding structures. Their location deep within the body precludes palpation of the tumor mass early in the course of the disease. Consequently, these tumors often reach a large size prior to diagnosis (Table 7.2).

On the other hand, visceral sarcomas or adenocarcinomas are less likely to achieve this large size prior to diagnosis because they cause intestinal dysfunction.⁵ The most common symptom is gastrointestinal bleeding (Table 7.3). Even though symptoms may arise earlier in the course of the disease, the anatomic location of these cancers is contiguous with the abdominal space. They frequently present with a regional disease process referred to as peritoneal sarcomatosis. For this reason, visceral (gastric, small bowel and colonic) sarcomas also carry a poor prognosis. A majority of gastrointestinal sarcomas (previously called leiomyosarcomas) are stromal sarcomas. The distribution of gastrointestinal stromal tumors is presented in Table 7.4.⁵

Table 7.1 Soft-tissue sarcomas by site (percentages)

Head and neck	9
Trunk	19
Retroperitoneum, pelvic sidewall, visceral	12
Upper extremity	13
Lower extremity	46

Table 7.2 Clinical presentation of retroperitoneal sarcomas (percentages)

Abdominal mass	80
Abdominal pain	60
Weight loss	35
Nausea, vomiting	20
Lower extremity edema	17
Urinary symptoms	3
Hypoglycemia	1

From ref. 4

Table 7.3 Clinical presentation of gastrointestinal sarcomas (percentages)

Symptom	Gastric	Small bowel	Large bowel
Bleeding	45	54	28
Mass	42	23	65
Pain	36	57	43
Nausea/vomiting	33	—	—
Weight loss	6	15	—
Change bowel habits	—	15	48
Asymptomatic	11	—	—

From ref. 5.

Table 7.4 Distribution of gastrointestinal stromal sarcoma (percentages)

Esophageal	5
Stomach	47
Small bowel	35
Colon	4
Rectum	17
<i>Total</i>	99

Modified from ref. 5.

Tumor Biology of Hematogenous versus Lymphatic Dissemination

The tendency to disseminate to lymph nodes is markedly different for sarcomas than for adenocarcinomas. Epithelial cancers (squamous cell carcinomas and adenocarcinoma) metastasize through both the lymphatic route and the hematogenous route. In contrast, mesenchymal cancers frequently enter the blood stream, causing lung or liver metastases, but rarely result in lymph node metastases. Overall metastatic involvement of regional nodes is observed in only 13% of patients with soft-tissue sarcomas and in 7% of bone sarcomas at initial presentation.⁶ Lymph node involvement by a sarcoma is unusual; when it occurs it indicates a dismal prognosis.

Direct evidence for the preferential hematogenous or lymphogenous dissemination of the two classes of tumors is based on numerous observations that regional lymph node metastases are more common in carcinomas than in sarcomas.⁷ Although nodal metastases do occur with sarcomas, they generate lymph node metastasis in a much smaller proportion of patients than do carcinomas. The explanation for this phenomenon from a tumor biology perspective has not yet been formulated. Are the observed differences in pattern of metastases due entirely to the properties of the cancer cells themselves? Could there be a greater destruction (metastatic inefficiency) of sarcomatous tumor emboli in lymphatics? Are the differences the consequence of a more intimate association of sarcomas than carcinomas with their vasculature? A new hypothesis is that the anatomic microenvironment of the primary tumor mass controls the proportion of tumors disseminating by hematogenous or by lymphatic routes.

Our knowledge of the intrinsic capabilities of sarcoma cells versus carcinoma cells to invade and then to metastasize is limited. We must accept that invasion must occur before metastases can occur. For both sarcomas and for carcinomas there must be sufficient invasion and sufficient progression for metastases to

result. From a histopathologic study of sarcomas and adenocarcinoma, both cancers have an intimate relationship with their blood supply. Breakdown of blood vessel walls and hemorrhage into tumor tissue may be a more impressive aspect of the histopathologic study of the sarcomas. Yet invasion of veins and venules is also a common pathologic finding with adenocarcinoma. The fact that both sarcomas and carcinomas disseminate via veins (hematogenous metastases) to distant capillary networks is not the issue. The discrepancy in patterns of dissemination concerns the relatively infrequent sarcomatous dissemination to lymph nodes.

Currently, no differences in the invasive capabilities of the primary tumor to penetrate capillary venules as opposed to lymphatic channels have been described. There is no reason to suspect that sarcomas selectively invade capillary venules versus lymphatic channels. Basic differences in the tumor biology of malignant mesenchymal versus malignant epithelial tumors do not explain the low rate of lymph node metastases observed for sarcomas.

Mesenchymal structures such as bone, striated muscle and smooth muscle have a very rich blood supply. It is not surprising that this blood supply is readily violated by tumor invasion, and venules are seeded by exfoliation of the cancerous process. However, mesenchymal structures have a severely limited lymphatic drainage system. From an evolutionary perspective the lymphatic system has evolved as a host defense against pathogens. Antigens gathered from epithelial (endodermal or ectodermal) structures are secured within the lymph nodes. Then through antigen processing, immunocyte selection and proliferation, a specific immune response is generated. There is a limited lymphatic supply for mesodermal structures because these soft tissues are rarely involved in host defense against invasion by pathogens. Lymphatic systems within the mesoderm are poorly developed, and what occurs may communicate less directly with the regional node groups that accompany the vasculature of the bowel or that drain to axilla or groin. The reduced lymphatic supply of bone, cartilage, muscle, fat and other mesenchymal tissues leads to a decreased exposure of lymphatic channels and lymph nodes to sarcoma metastases.

In summary, the hypothesis is that fewer lymph node metastases occur in patients with sarcomas because fewer lymphatic channels are at risk for invasion and embolization by the primary malignancy. [Table 7.5](#) relates the lymphatic supply of the tissue of origin of carcinomas and sarcomas to the incidence of lymph node metastases. Bone does not have lymphatic channels and therefore osteosarcoma rarely shows lymph node metastases. Rhabdomyosarcomas occur within

Table 7.5 Relationship of lymphatic supply of the tissue of origin to the incidence of lymph node metastases

<i>Tumor type</i>	<i>Tissue of origin</i>	<i>Lymph supply tissue of origin (0–4+)</i>	<i>Lymph node metastases (%)</i>
Osteosarcoma	Bone	±	5
Liposarcoma	Fat	±	5
Gastrointestinal stromal tumor	Purkinje plexus	±	5
Rhabdomyosarcoma	Striated muscle	2+	20
Epithelioid sarcoma	Skin appendages	2+	20
Gastric carcinoma	Gastric epithelium	4+	50
Melanoma	Skin	4+	50

muscle. Muscle has an intermediate number of lymphatic channels and consequently there are moderate numbers of lymph nodes involved by this cancer. Epithelioid sarcomas involve lymph nodes relatively frequently. As predicted, these tumors are very common on the hands, involve the subcuticular dermis and have access to the rich lymphatic plexus at these sites. The higher incidence of metastases in epithelioid sarcomas is to be expected because of the rich lymphatic supply of the skin.

Tumor Biology of Local–Regional Recurrence of Sarcoma

Another feature characteristic of the natural history of sarcomas involving the abdomen or pelvis is the alarmingly high local recurrence rate. The major site for surgical treatment failure is the same anatomic area from which the sarcoma was removed. Local recurrence is a component of treatment failure in nearly 100% of patients and is the only site of treatment failure in nearly 50% of patients.^{8,9} One factor to be considered as a cause of local recurrence is a multifocal primary tumor (Figure 7.1). This phenomenon may be especially prominent with retroperitoneal liposarcoma. A second factor that will cause local recurrence is small foci of tumor (satellite nodules) present at a distance from the primary sarcoma. Narrow margins of resection may cause cancer persistence of these satellite sarcoma deposits within the resection site. With time these small foci of cancer will progress; also, their growth may be promoted by the wound-healing process. However, in a majority of patients the high rate of local and regional recurrence comes about as a result of sarcoma seeding at the resection site and on peritoneal surfaces. Intraperitoneal sarcoma emboli may occur as a result of: (1) sarcoma penetration of the peritoneal layer with release of tumor emboli into the peritoneal space

preoperatively; (2) sarcoma emboli in venous blood that is lost into the abdomen at the time of surgery; (3) surgical trauma that causes a sarcoma spill into the abdominal cavity. These free intra-abdominal tumor emboli become entrapped in fibrinous exudate that floods the traumatized surfaces involved in the surgical dissection. This outpouring of serosanguinous fluid is the first phase of the wound-healing process. After the fibrin becomes organized into a coagulum, tumor cells are trapped at the wounded site. Platelets and mononuclear cells infiltrate the fibrinous matrix and release copious amounts of growth factors. These soluble mediators result in the proliferation of normal cells and modulate the healing process.

Recurrence at the resection site of a visceral sarcoma or retroperitoneal and pelvic sidewall sarcoma usually has a fusiform gross appearance. This characteristic progression along the narrow margins of resection is most frequently caused by high-density sarcoma seeding of intraperitoneal cancer cells. Sarcoma emboli are also likely to adhere at a lower density to traumatized peritoneal surfaces where they become covered by a fibrinous exudate. These peritoneal surface implants progress as individual sarcoma nodules that may be widely distributed throughout the abdomen and pelvis. In summary, high-density seeding of sarcoma emboli at the resection site results in local recurrence that has a fusiform gross appearance. Low-density seeding of sarcoma emboli on peritoneal surfaces causes sarcomatosis. These nodules will usually occur within adhesions because the sarcoma emboli were entrapped at that site by fibrin.

The growth factor stimulation as a result of wound healing results in accelerated local progression of the sarcoma emboli; also, further sarcoma dedifferentiation may result from the exposure of sarcoma cells to growth factors.¹⁰ It is well established that the invasive potential of sarcomas may dramatically increase over time as a result of multiple reoperations.

Mechanisms of Local Recurrence and Peritoneal Sarcomatosis

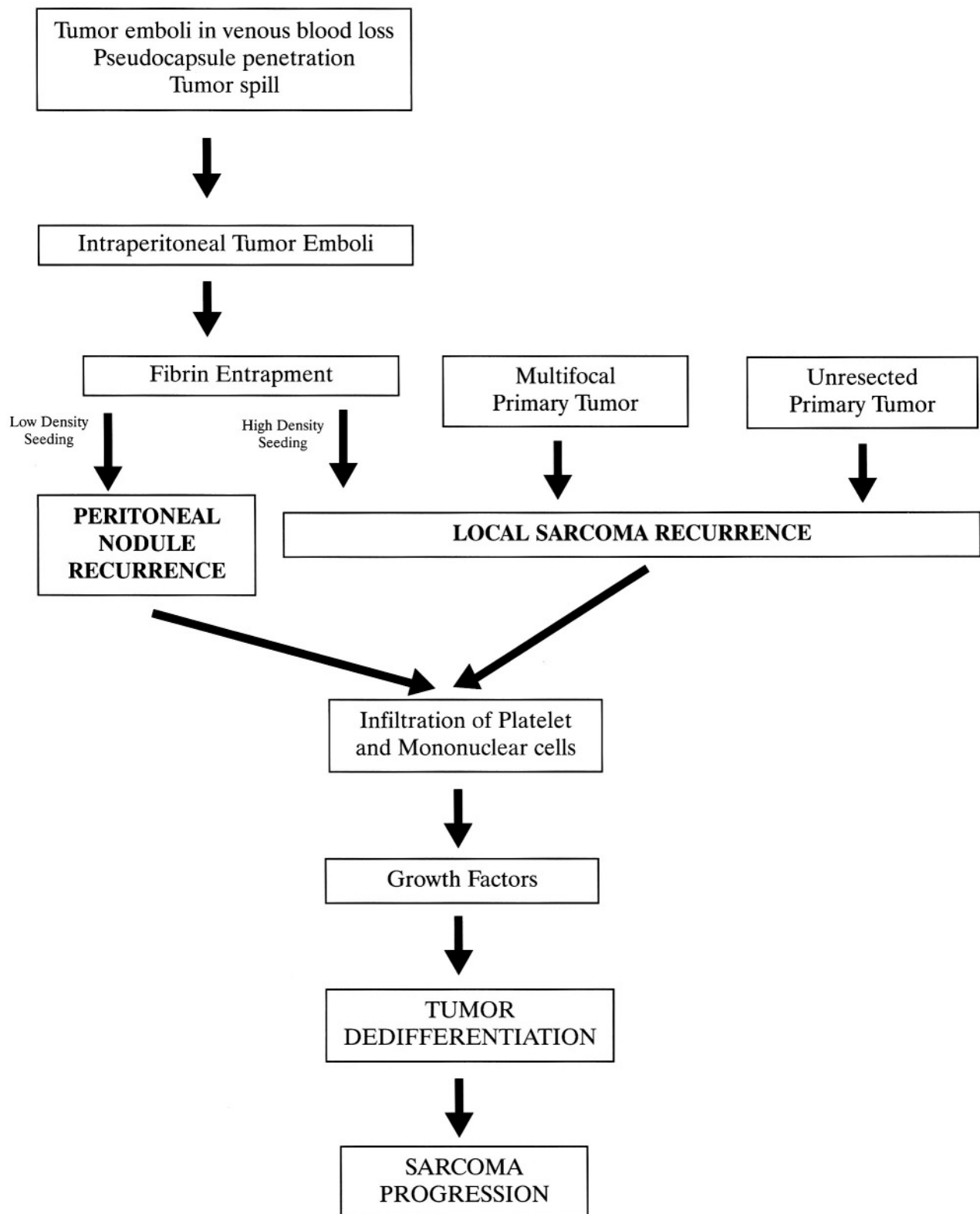


Figure 7.1 Factors contributing to the high rate of local recurrence of sarcomas involving the abdominal and pelvic cavity.

Tumor Biology of Peritoneal Sarcomatosis

After resection site recurrence the second most common sites for abdominal or pelvic sarcoma recurrence are the peritoneal surfaces.^{8,9} In some patients sarcoma seeding of the peritoneum will have occurred prior to resection of the primary tumor and is documented upon exploration of the abdomen. In the reoperative setting, peritoneal sarcomatosis results from tumor emboli in venous hemorrhage or from tumor spill that occurred with a prior sarcoma resection.¹¹ As implied from Figure 7.1, the distribution of sarcomatosis favors sites of prior peritoneal trauma. Sarcoma deposits are expected to grow out from single cancer cells trapped within abdominal adhesions. Of course, these adhesions develop with the resolution of fibrinous deposits that result from previous surgical trauma. The pathobiology of peritoneal implantation suggests that multiple factors control the distribution of cancer seeding within the abdomen and pelvis and that this is not a random event.¹²

Hematogenous Seeding to Lungs versus Liver

A difference in the intravascular dissemination of extremity sarcoma, retroperitoneal and pelvic sidewall sarcoma on the one hand and visceral sarcoma on the other needs to be noted. The first capillary bed draining the primary tumor is at highest risk for sarcoma metastasis.⁷ For extremity sarcoma this is the lungs. For retroperitoneal and pelvic sidewall sarcoma the capillary bed at increased risk is also the lungs. For visceral sarcoma the venous blood draining the cancer is the portal system. With these malignancies the liver is by far the most common site for hematogenous metastases.

Figure 7.2 summarizes the patterns of treatment failure of sarcomas involving the abdomen and pelvis. The diagram emphasizes the high local recurrence rate and indicates that peritoneal seeding of sarcoma is a component of local recurrence. The first capillary bed draining retroperitoneal and pelvic sidewall sarcomas are the lungs; for visceral sarcomas this capillary bed is the liver. Neither group of sarcomas metastasizes to lymph nodes in a significant proportion of patients.

TREATMENT

Enneking and colleagues have emphasized that there are two basic principles by which the treatments for sarcoma are directed.¹³ First, one must determine as precisely as possible the anatomic location of the tumor. The second determinant for treatment of sarcoma concerns the biologic aggressiveness of the malignant process. With knowledge of these two determinants, cancer treatments can be selected that have the greatest likelihood of destroying the lesion with minimal compromise of normal function and quality of life. Low-grade lesions can be treated with a high expectation for cure even with minimal surgical margins. Also, one does not need to consider any therapies in addition to surgery for low-grade lesions excised with negative surgical margins. On the other hand, aggressive sarcomas must be expected to invade more deeply into the adjacent tissues, can produce satellite lesions in the surrounding soft tissue, and are capable of metastasizing via hematogenous routes to distant sites. Knowledge of the low biologic aggressiveness of a disease process in an advanced stage may encourage ultraradical regional treatments. At other times the futility of highly morbid therapies will become evident,

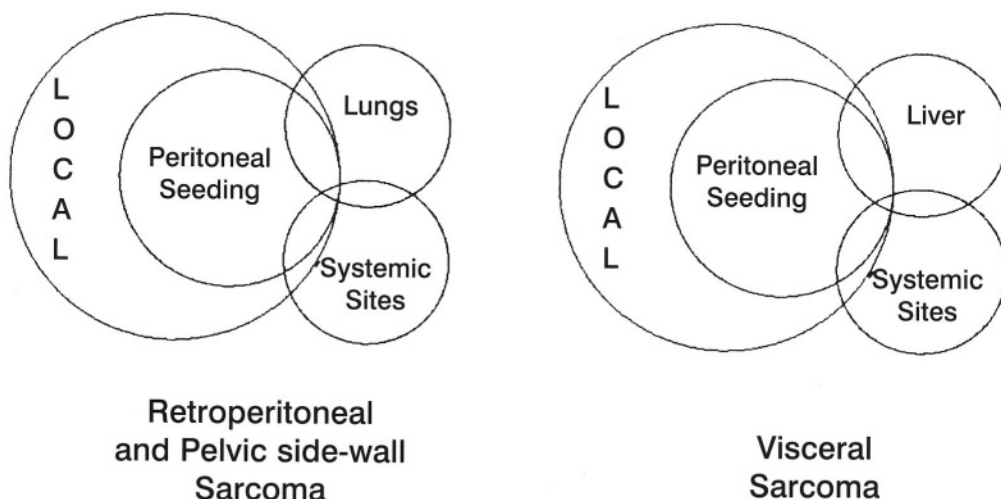


Figure 7.2 Surgical treatment failures of abdominal and pelvic sarcomas.

and an aggressive lesion of large volume will be treated with conservatism because the clinician's judgement has determined that it is an incurable process.

In dealing with abdominal and pelvic sarcomas one should realize that the routes for cancer dissemination are considerably different from those of adenocarcinomas. The adenocarcinomas require wide excision of the draining lymphatic tissues because lymph node metastases are common and the excision of involved nodes can result in cure. In contrast, lymph node involvement with abdominal and pelvic sarcoma is unusual, and if it does occur excision of the involved nodes will rarely result in long-term survival. Lymph node positivity in patients with sarcoma is almost always regarded as a signal of an unusually aggressive cancer, and it is highly probable that there has been systemic dissemination of disease. Consequently, in dealing with these sarcomas one attempts to remove the tumor with a generous margin of normal tissue, but wide lymph node dissections are unnecessary.¹⁴

Our comments will focus on the treatment option that have demonstrated efficacy in the management of abdominal and pelvic sarcomas. The first priority for treatment is surgery with negative margins of excision.¹⁵ The results of surgical treatment alone are shown in Figure 7.3. The more recent addition to abdominopelvic treatment options is intraperitoneal chemotherapy.¹⁶⁻¹⁸ Radiotherapy has not shown survival benefits when used as an adjuvant with surgery^{19,20}; also, aggressive systemic chemotherapy combined with surgery has no demonstrated survival benefits.²¹

Surgical removal with a clear margin is the treatment option indicated for all abdominal and pelvic sarcomas. This approach will test the surgeon's ability to exercise all those principles of surgery which allow large operations to be performed with minimal morbidity and mortality. Successful surgical treatments demand optimal exposure, skill in dealing with intestinal adhesions, meticulous hemostasis that is maintained throughout the procedure, a thorough knowledge of anatomy, a plan of attack on sarcomas at difficult anatomic sites and experience in reconstruction. The surgeon must be knowledgeable regarding those structures that can be sacrificed because of their involvement by tumor, and those structures that must be preserved even if there is residual sarcoma.

SURGICAL APPROACH

At this point in time the first priority for treatment for abdominal and pelvic sarcoma that is associated with long-term survival is complete surgical removal of the cancer with adequate margins. The cardinal principle of surgery is en-bloc excision of the primary tumor plus involved adjacent organs and tissues with dissection

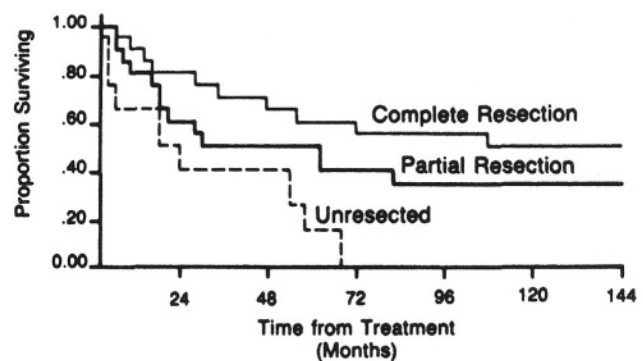


Figure 7.3 Actuarial survival for retroperitoneal sarcomas. Only complete resection achieves any hope for long-term survival. The expected survival for complete resection shows approximately 50% survival at 5 years. Unresected patients have a uniformly poor prognosis. Some patients with positive margins of resection who have grade I or less sarcomas will survive long term; often these patients live with gradually progressive cancer and require multiple resections over a long time period. From Jaques DP, Coit DG, Brennan MF. Soft tissue of the retroperitoneum. In: Shiu MH, Brennan MF, editors. *Surgical Management of Soft Tissue Sarcomas*. Philadelphia: Lea & Febiger; 1989:166.

well clear of the sarcoma pseudocapsule. The major factor determining resectability is the extent of invasion to vital structures rather than the size of the tumor. Although preoperative radiological evaluation is essential, operability can be evaluated definitively only by laparotomy. Even with adherence of tumor to vital structures, with meticulous dissection most sarcomas are resectable. The surgeon must always remember that inadequate clearance resulting in local recurrence and inadequate containment resulting in sarcoma seeding are the major causes of treatment failure. Tumor debulking may occasionally be beneficial in a palliative way in cases where complete resection is impossible. However, palliative surgery for abdominal and pelvic sarcoma carries a high morbidity and limited progression-free survival and should be undertaken with great caution.

Patient Position and Exposure

One must be prepared for a major surgical event with wide abdominal and pelvic exposure in order to achieve the greatest incidence of success. In many patients both abdominal and pelvic dissections must be performed. Positioning of the patients so that surgery through the perineum is possible is often indicated (Figure 7.4). Long abdominal incisions from xiphoid to pubis are usually required. Self-retracting retractors that can expose the entire abdomen and pelvis are necessary

(Figure 7.5). Skin preparation for a thoraco-abdominal or an abdomino-inguinal incision is frequently required (Figure 7.6).

One must always be cognizant of the surgeon's needs to think three-dimensionally in approaching these deep-seated malignancies. This helps to avoid inadvertent damage to vital structures. In order to build within the surgeon's mind a three-dimensional appreciation of the vital structures in the abdomen, one should always strive to open the abdomen and set up

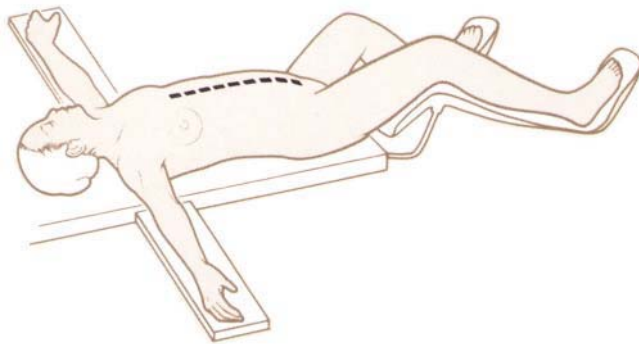


Figure 7.4 Patient position for surgical treatment of abdominal and pelvic sarcoma.

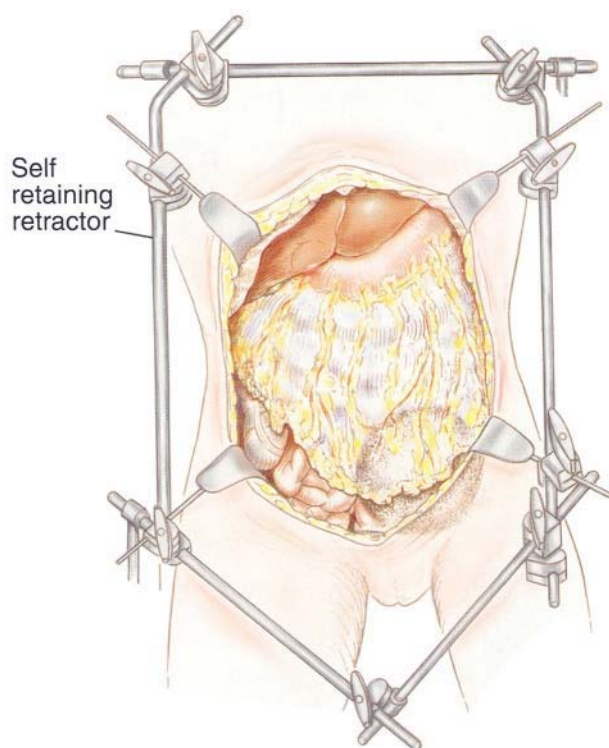


Figure 7.5 Exposure for abdominal and pelvic surgery using a self-retaining retractor.

the self-retaining retractor system in the same way. This means that vital structures such as the left common iliac vein, the ureters, the left gastric artery, and the common bile duct have a particular spatial orientation within the surgeon's mind. A standard exposure of the abdominal cavity through a midline incision with uniform placement of the self-retaining retractor can assist the surgeon in his goal of avoiding hemorrhage and inadvertent damage to vital structures.

Reoperative Surgery

Frequently, in a tertiary referral center, one sees patients with abdominal and pelvic sarcomas after one or more prior attempts at the surgical removal of the cancer. In these patients, removal of the recurrent sarcoma may be delayed many hours because exposure of the tumor mass may be difficult and time-consuming. Extensive abdominal adhesions, tumor that has regrown within scar tissue, fibrosis that accompanies the local recurrence of cancer, and alterations of normal anatomy by prior reconstructions may require patience and advanced technical skills to bring about the complete exposure of the malignant process.

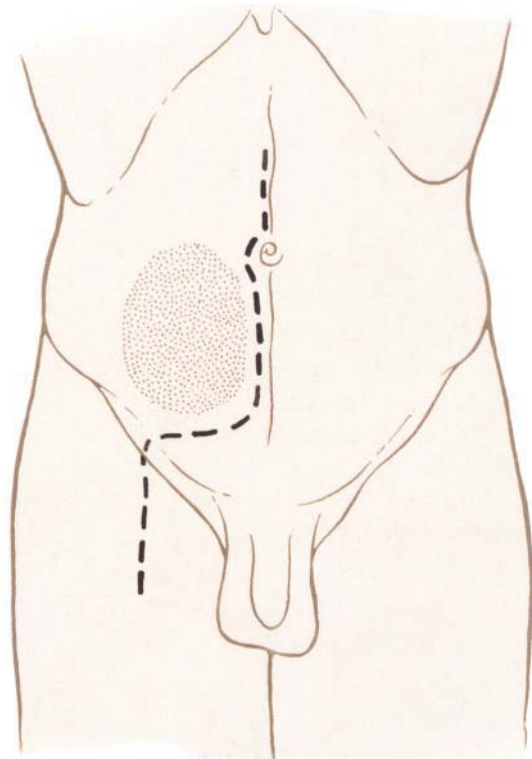


Figure 7.6 Abdomino-inguinal incision used for resection of sarcomas on the pelvic side wall.

Always Open Old Incisions

Even though opening an old incision is difficult, and may result in seromuscular tears of small or large bowel, rarely should a new incision be made into the abdomen in performing reoperative surgery. New incisions will cause additional adhesions and may severely jeopardize primary wound healing of the abdominal wall. It is usually necessary to excise old incisions because they often contain recurrent sarcoma embedded within the scar tissue. The surgeon routinely plans to completely excise the old scar tissue in the skin, subcutaneous tissue and in fascia as the abdominal wall is opened.

Safe Entry into the Abdominal Cavity

Opening the abdomen without damage to bowel in a patient who has had several prior surgical procedures is difficult and time-consuming. One should realize that entering an abdomen with multiple adhesions requires an *elevation* of the abdominal wall in order to avoid inadvertent small bowel or large bowel enterotomy. Clamps should be used to apply strong upward traction on the skin or abdominal fascia as the abdomen is entered (Figure 7.7). Pushing down in order to spread the scar that makes up the old abdominal incision is to be avoided.

Surgical Approach to Intra-abdominal Adhesions

Small bowel adhesions present a special problem in management. Small bowel enterotomy resulting in fistula formation after reoperative procedures is a major problem that will be encountered. The experienced surgeon will adhere to several principles in lysing small bowel adhesions:

1. Tactile sense should be added to visual perceptions in the dissection of the adhesions (Figure 7.8). This requires the use of ball-tipped electrosurgery. Fibrous adhesions and fat are morseled between the thumb and index finger of the nondominant hand. Considerable pressure may need to be applied. Ball-tip electrosurgery electroevaporates (carbonizes) residual tissue on the small bowel surface as this tissue is splayed out on the middle finger.
2. Absolute hemostasis must be maintained at all times in dissecting small bowel adhesions. One must realize that any bleeding that occurs while dissecting a small bowel adhesion means the surgeon is in an improper plane. Fat with blood vessels within should be divided in the abdomen and pelvis only when the surgeon is knowingly transecting omentum, transecting retroperitoneal structures, or transecting perirectal fat. Bleeding that is encountered while taking down intestinal adhesions indicates that the surgeon is dissecting within the wrong plane,

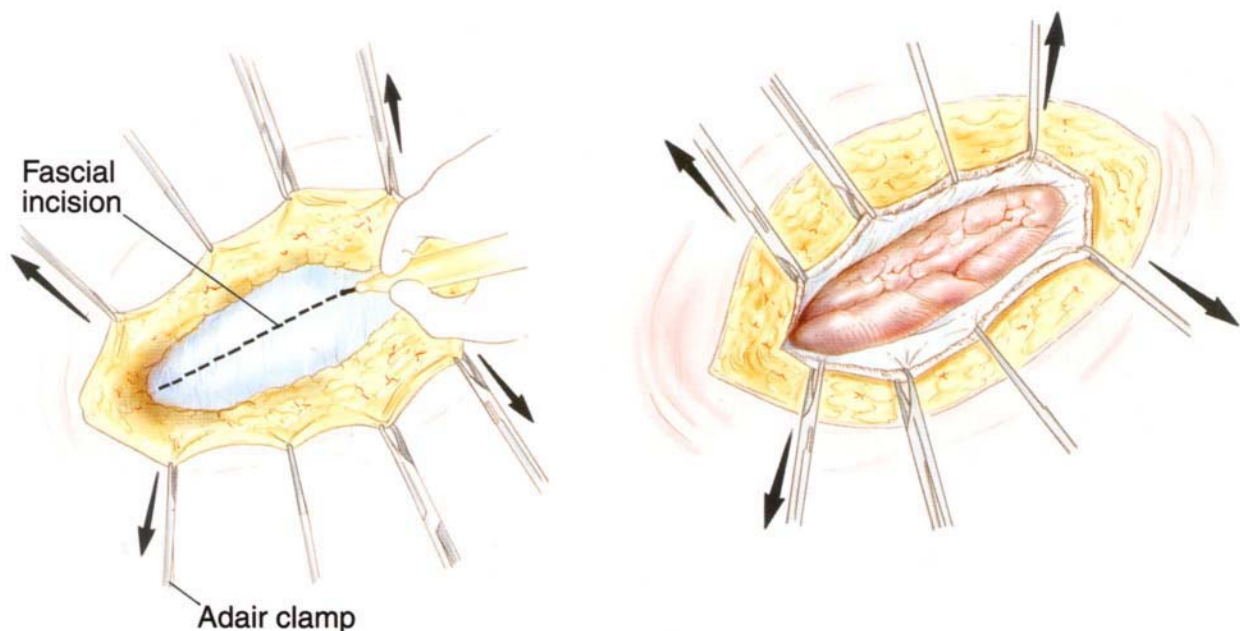


Figure 7.7 Opening the old abdominal incision by pulling upward on skin (left) or fascial edges (right) using Adair clamps.

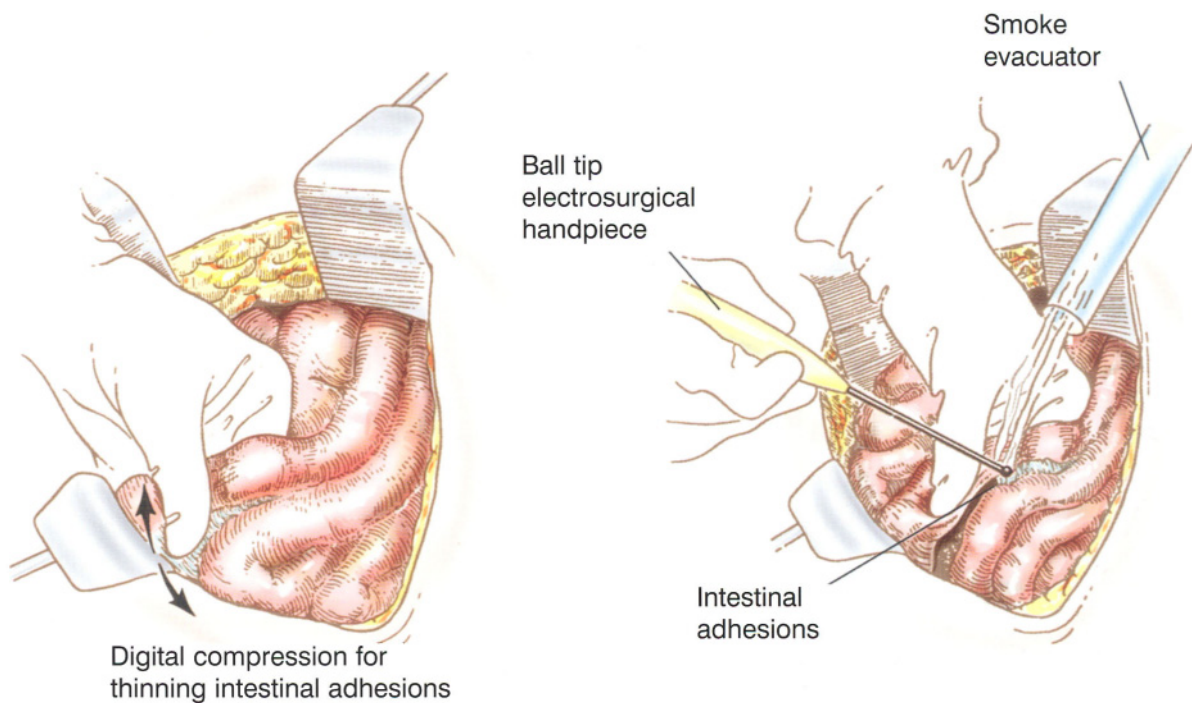


Figure 7.8 Dividing abdominal adhesions. Pressure between thumb and index finger is used to thin out the adhesion between two loops of small bowel. Ball-tip electrosurgery is used to divide and evaporate the adhesion (right). Division of adherent tissue on small bowel surfaces on the middle finger of the nondominant hand adds tactile to visual perceptions (left).

usually the small or large bowel mesentery, and this should be avoided.

3. Large-volume saline irrigation should be used frequently. Even small amounts of blood can interfere with adequate visualization of subtle tissue planes for further dissection. If absolute hemostasis is combined with frequent irrigation the translucent nature of the tissues will be preserved throughout the dissection and inadvertent damage to vital structures or to blood vessels should not occur.
4. Fat or scar tissue should never be left behind on small bowel surfaces. This scar tissue may frequently contain entrapped tumor cells. Also, if miscellaneous tissues remain on bowel surfaces, confusion may arise in subsequent dissection. There is only one small bowel surface that contains fat on its anti-mesenteric border, and this is in the terminal ileum.
5. Strong traction should be maintained at the dissection point of the adhesion. The small bowel should be splayed out (broad traction) so that the plane of dissection for the ball-tipped electrosurgical handpiece is clearly visualized.
6. Complete removal is the rule when dealing with intra-abdominal adhesions. Generally, all adhesions must be lysed and then resected. The complete anatomy of the large and small bowel is visualized

prior to a decision regarding curative versus palliative sarcoma resection.

In summary, in the reoperative setting opening old abdominal incisions and the dissection of abdominal adhesions without damage to the bowel must be mastered by the sarcoma surgeon. Use of electrosurgery with the ball-tip is indicated because it allows tactile sensations to be added to visual perceptions in the dissection. This makes the process safer and certainly expedites the opening of the abdomen, lysis of intra-abdominal adhesions and clarification of the dissection required for definitive excision of the recurrent sarcoma.

Exploring for Sarcomatosis

In performing surgery on patients with retroperitoneal or visceral sarcoma, the complete (both visceral and parietal) abdominal and pelvic surfaces must be visually inspected to look for tumor deposits. This means that all abdominal adhesions must be lysed as part of the complete exploration. The omentum, likewise, must be dissected free and inspected to determine whether it contains sarcoma nodules. The problem of sarcomatosis is of course more important in patients undergoing reoperative surgery for intra-abdominal sarcoma. If

there was tumor spillage at the time of earlier surgery, then sarcomatosis is expected to be discovered with the abdominal exploration.

If the patient can be made disease-free in the presence of sarcoma nodules, then the benefits of intraperitoneal chemotherapy should be considered. The adhesions are completely separated and resected as part of the oncologic procedure to allow uniform distribution of chemotherapy. From a purely surgical point of view, complete lysis and resection of all abdominal adhesions is not an absolute requirement for safe resection of abdominal and pelvic sarcoma. From an oncologic perspective, complete lysis and resection of all adhesions followed by perioperative intraperitoneal chemotherapy may be an absolute requirement for the prevention of subsequent sarcomatosis.

Centripetal Dissection

Centripetal dissection requires wide continued exposure of the abdomen and pelvis as provided by a long midline abdominal incision and self-retaining retractors. Repeated dissection in a circular fashion around the principal tumor mass at multiple sites is the goal. Dissection continues at a particular site only if there is clear visualization of the operative field. The surgeon should repeatedly circle the sarcoma as the laborer would repeatedly circle a tree stump that is being removed with shovel and axe. The "stump analogy" suggests that the surgeon never attempts a definitive dissection in one area. He always completes the superficial dissections before the more difficult deep ones are attempted. The axiom is always "Do what is easy first." He moves around and around the cancer, working only where he has good exposure. Criteria for continued dissection at a particular anatomic site include: (1) no loss of blood; (2) small chance for damage to vital structures; (3) dissection proceeding with a clear margin. If any of these criteria for safe progress are not met, the surgeon should move his dissection to a different area. The tumor mass is generally circled many times prior to delivering the intact specimen. In summary, centripetal dissection avoids at all times major hemorrhage or damage to vital structures by limiting dissection to areas that allow clear visualization of the operative field. A circular pattern of progressively deeper dissection results from this approach.

Avoid Trauma to the Vasculature of the Sarcoma Capsule

In the removal of abdominal and pelvic sarcomas one must always be aware of possible major hemorrhage

from surface vasculature of the sarcoma. Blood vessels in the sarcoma pseudocapsule are large, thin-walled, easily traumatized and difficult to control once bleeding has occurred. Once one disrupts the tumor vasculature, bleeding is likely to be brisk. One should dissect away from the tumor in normal tissues as much as possible. If dissection of the tumor itself is required, this should be done only after all other dissection is completed.

Maintain Hemostasis throughout the Procedure

One must always pay continuous attention to hemostasis, because inadequate hemostasis interferes with subsequent exposure. Moreover, blood in the operative field obscures the identification of additional bleeding points. Hemostasis must be achieved with electrocoagulation, ligatures, or clips as the dissection proceeds. The translucent nature of the tissues within the surgical field can be maintained by frequent irrigation and meticulous hemostasis.

Use of Peritonectomy Procedures

Often in the reoperative setting or with a retroperitoneal sarcoma the surgeon must be willing to dissect in a preperitoneal or retroperitoneal plane rather than moving through the peritoneal cavity itself. Peritonectomy procedures go beneath scar tissue to achieve a negative margin of resection.²² Sarcoma recurrent at a resection site will almost always be beneath the peritoneal surface. An effective way to safely approach these recurrent tumor masses is by going beneath the peritoneal layer into a deeper plane away from the tumor mass (Figure 7.9). The concept of peritonectomy should be pursued in the reoperative setting, in dealing with sarcomatosis, with recurrence at the resection site, and for retroperitoneal sarcoma being resected for the first time.

Utilize "Piecemeal" Excision

Often freeing-up of a tumor mass will progressively obscure the plane of dissection. This will compromise the safety of subsequent dissection because of inadequate visualization, inadequate hemostasis, or an unnecessarily narrow margin of excision. Large tumor masses, especially those in the pelvis, will become more and more difficult to extirpate as the dissection proceeds. As the anatomic site for further dissection is more deeply obscured by a large mass of tumor, the procedure becomes more dangerous. If the tumor mass remains intact, dangerous blunt dissection may be required to continue its removal.

In this situation, piecemeal excision of the sarcoma is an important part of the operative procedure. Superficial components of the tumor may be removed prior to continuing the dissection of a deeper aspect of the tumor. Piecemeal excision using an electrosurgical loop on pure cut is usually the best way to remove portions of the tumor prior to its complete resection (Figure 7.10).

Piecemeal excision of a large tumor mass is much safer for the patient than is dissection with inadequate visualization. However, one must do everything possible to guard against the intra-abdominal dissemination of sarcoma cells. The surrounding structures must be protected with laparotomy pads and towels. The electrosurgical loop at high voltage on pure cut removes fillets of tumor with minimal spillage of viable malignant cells. After each level of tumor is resected, thorough irrigation of the operative field is required. Before the procedure is completed intraperitoneal chemotherapy is indicated.

Guard against Frustration Toward the End of a Difficult Resection

The surgeon should realize that the greatest number of surgical misadventures occur just a few minutes prior to final removal of the tumor mass. Special care should be taken when the tumor mass is almost out. The final dissection is often performed over a large mass of sarcoma that results in reduced visualization. One must avoid damage to a vital structure such as a ureter or damage to a major blood vessel which results in

profuse hemorrhage. Many serious intraoperative errors in cancer resection occur just prior to the removal of a large specimen.

Transplants of Primarily Vascularized Tissue

Within the abdomen there are two prominent sources of primarily vascularized tissue. These are the omentum and the rectus abdominus muscles. The rectus abdominus muscles based on the deep inferior epigastric vessels can be harvested either bilaterally or unilaterally (Figure 7.11). The omentum can be harvested so that its gastroepiploic pedicle is based on the left gastroepiploic vessels and the short gastric vessels on the left side of the stomach. More frequently the omental pedicle is based on the right side from the right gastroepiploic vessels (Figure 7.12). In both instances the numerous branches of the gastroepiploic vessels to the greater curvature are ligated and the gastroepiploic arcade is preserved. These large masses of freshly vascularized tissue can be used in four ways.

The primarily vascularized tissue is frequently used to fill empty space in the abdomen or pelvis. This tissue is often placed into an abdominal gutter from which a kidney was removed or into the pelvis. This greatly facilitates healing and serves to decrease the incidence of fluid accumulation and possible pelvic sepsis. These tissue transplants greatly improve the healing at a site of prior radiotherapy.

A second use of pedicle flaps is to create a new abdominopelvic partition. This tissue barrier does not

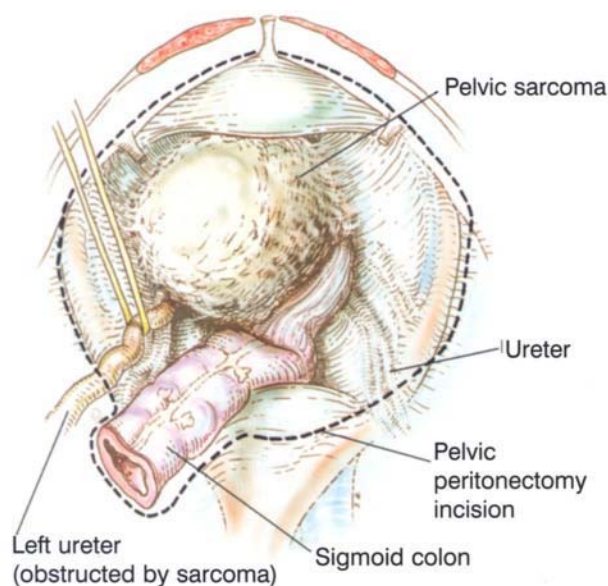


Figure 7.9 Pelvic peritonectomy is useful to completely excise a pelvic sarcoma, especially if there is sarcomatosis or recurrent tumor at the resection site.

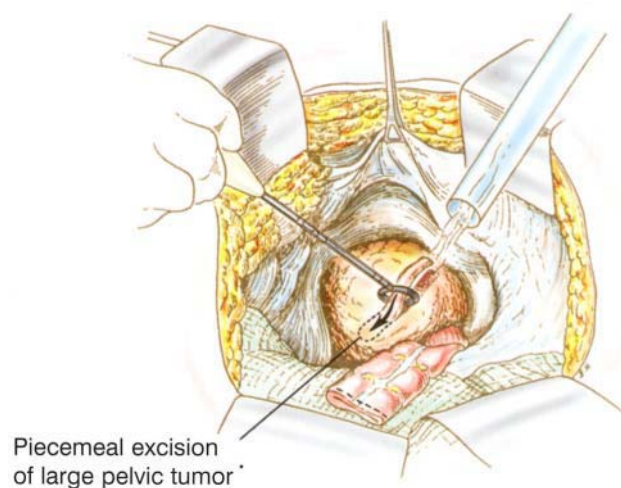


Figure 7.10 Piecemeal excision of abdominal or pelvic sarcoma. Electroevaporative surgery with a ball tip is used to define the margin of excision. Loop electrosurgery is used to resect the sarcoma mass piecemeal. Even in the depths of the pelvis with a large sarcoma the visualization can be excellent.

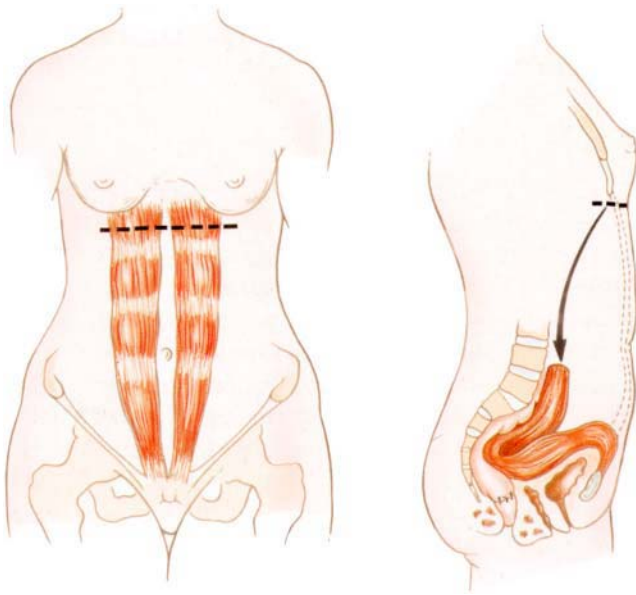


Figure 7.11 Primarily vascularized tissue transplant of rectus abdominis muscles. These are especially needed if the patient has had prior radiation therapy to the pelvis.

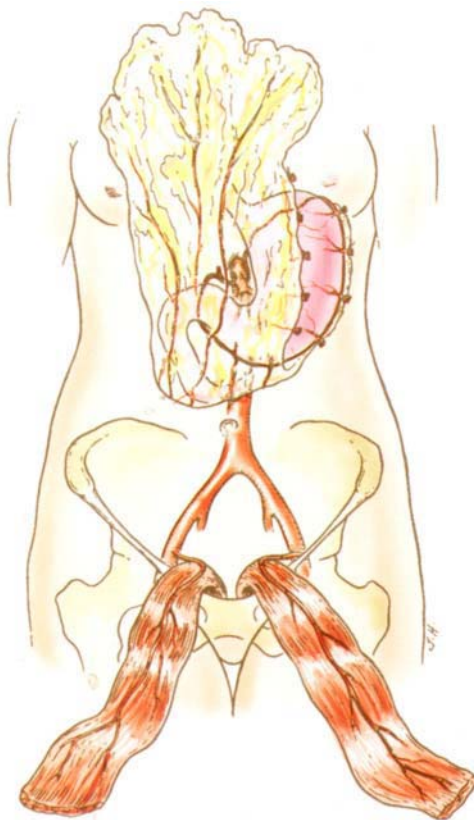


Figure 7.12 Primarily vascularized tissue transplants may be harvested from three sources for abdominal and pelvic surgery. They are the greater omentum, right rectus muscle and left rectus muscle.

allow small bowel to become entrapped in the pelvis, resulting in subsequent intestinal obstruction or fistulization. Other sources of tissue can also be used in construction of an abdominopelvic partition. Bladder, uterus, leaf of sigmoid mesentery and prosthetic materials have been used successfully (Figure 7.13).

A third common need for these primarily vascularized tissue transplants is coverage of cancerous tissues that have been incompletely excised. Positive margins of sarcoma resection are walled off from the remainder of the abdominal or pelvic cavity by the primarily vascularized tissue transplant. This will greatly improve long-term function by preventing cancerous invasion of the small bowel and the resultant intestinal obstruction.

A fourth use of these primarily vascularized tissue transplants is to cover vascular grafts, reconstructed vessels, urinary tract reconstruction, or repair the bladder. Omentum or muscle draped over an exposed vascular graft or vascular anastomosis will protect against false aneurysm, graft infection, and suture line disruption with late blow out (Figure 7.14).

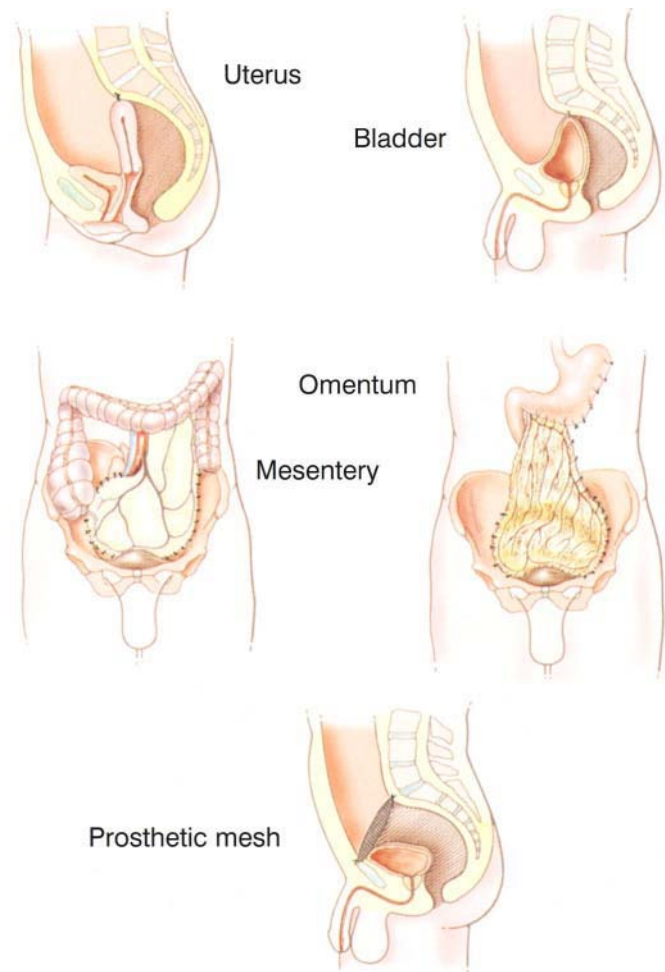


Figure 7.13 Methods to construct abdominopelvic partitions.

Induction Chemotherapy

External beam radiation therapy and adjuvant chemotherapy have failed to show worthy survival benefits for intra-abdominal sarcoma when added onto surgery. However, induction chemotherapy treatments designed to shrink large retroperitoneal or visceral tumors prior to their surgical removal is a treatment option applicable to selected patients (Table 7.6). Whenever there is a major single artery supplying the sarcoma, induction chemotherapy is used intra-arterially to maximize responses in the primary tumor itself. The goal of these treatment strategies is to shrink the tumor and reduce its aggressive behavior for a defined time period. After completion of induction chemotherapy excision of the malignant process may be possible

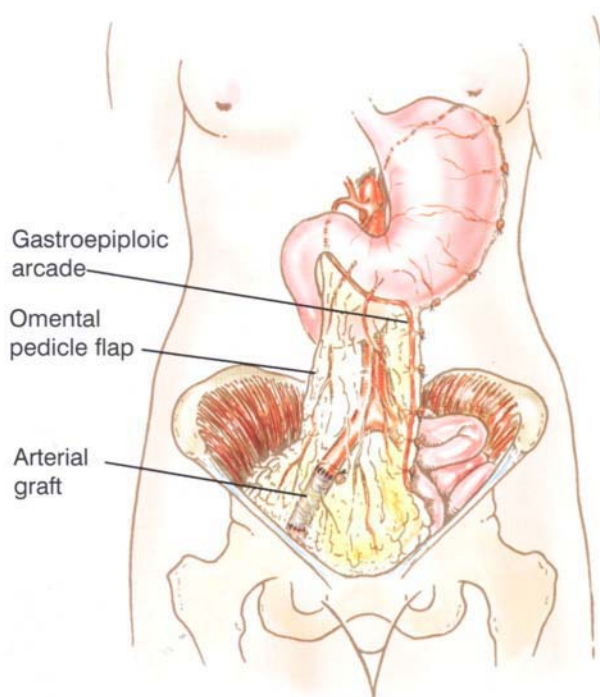


Figure 7.14 Omental pedicle flap used to cover common iliac artery reconstruction.

whereas surgery alone would have been unsuccessful. The current treatment plan utilizes three preoperative cycles of ifosfamide and systemic doxorubicin prior to surgical resection of the sarcoma.

Peritonectomy and Intraperitoneal Chemotherapy

Another strategy of great value in selected patients concerns the treatment and prevention of resection site recurrence and peritoneal sarcomatosis. Heated intraperitoneal chemotherapy employed intraoperatively is effective in reducing the high incidence of resection site recurrence and sarcomatosis that often occurs after primary sarcoma resection. Elimination of sarcoma seeding by peritonectomy and the resulting improvement in local-regional control may have an effect on the survival of patients with sarcomatosis or with local recurrence. Standardized orders for heated intraoperative intraperitoneal chemotherapy are shown in Table 7.7. Figure 7.15 shows the tubes and drains required to deliver early postoperative intraperitoneal chemotherapy. Figure 7.16 shows the methodology for safe intraoperative delivery of heated cisplatin and doxorubicin via the intraperitoneal route.

The indications for perioperative intraperitoneal chemotherapy are shown in Table 7.8. Tumor spillage should in all instances be accompanied by heated intraoperative intraperitoneal chemotherapy. Sugarbaker and colleagues, and Eroglu and colleagues, have used intraperitoneal cisplatin and doxorubicin.^{16,17} Other groups have explored the use of mitoxantrone.¹⁸ It should be emphasized that the prevention of peritoneal sarcomatosis is a surgeon's responsibility. Treatment of this component of sarcoma cannot be delayed until later systemic chemotherapy treatment by the medical oncologist. Once sarcoma cells are embedded in scar tissue they are not treatable by any technique. Other indications for intraoperative intraperitoneal chemotherapy include small-volume peritoneal sarcomatosis; small-volume residual disease on peritoneal surfaces or at the margins of resection; and use in a randomized control trial in patients who have a complete excision of

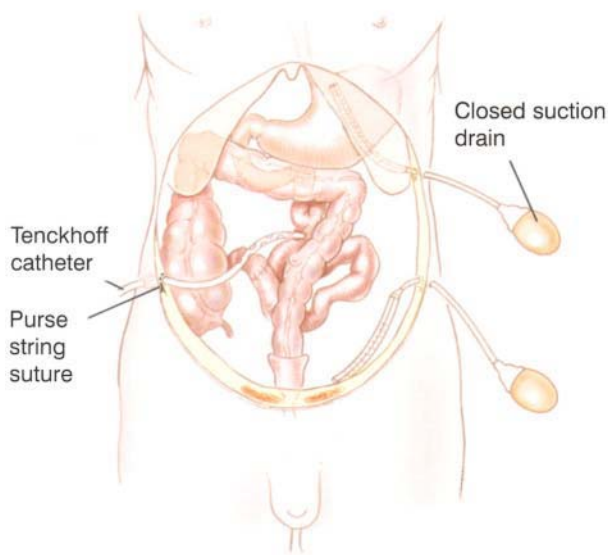
Table 7.6 Standardized orders for induction chemotherapy of abdominal and pelvic sarcoma

Induction ifosfamide and doxorubicin

1. Ifosfamide __ mg (2.25 g/m^2) intravenous for 4 consecutive days in 250 cc 5% dextrose solution via intravenous catheter as 2-hour infusion. Repeat every 3 weeks.
2. Doxorubicin __ mg (75 mg/m^2 per day) in 500 cc 5% dextrose in water to run by continuous intravenous catheter infusion through a central vein over 72 hours.
3. 25% dose reduction for both ifosfamide and doxorubicin for age greater than 65 or prior radiation therapy.
4. All cycles of chemotherapy are supplemented with G-CSF support at $5 \mu\text{g/kg}$ subcutaneous, starting 24 hours after chemotherapy is finished.

Table 7.7 Cisplatin and doxorubicin orders for heated intraoperative intraperitoneal chemotherapy

1. For gastric and ovarian cancer, mesothelioma and sarcoma; add cisplatin ___ mg to 2 liters of 1.5% dextrose peritoneal dialysis solution. Dose of cisplatin 50 mg/m².
2. Add doxorubicin ___ mg to same 2 liters of 1.5% dextrose peritoneal dialysis solution. Dose of doxorubicin 15 mg/m².
3. Use 33% dose reduction for heavy prior chemotherapy, marginal renal function, age greater than 60, extensive intraoperative trauma to small bowel surfaces, or prior radiotherapy.
4. Send 1 liter of 1.5% dextrose peritoneal dialysis solution to test the perfusion circuit.
5. Send the above to operating room ___ at ___ o'clock.

**Figure 7.15** Tubes and drains used for perioperative intraperitoneal chemotherapy.

sarcoma in order to identify a surgical adjuvant treatment.

The results of treatment of patients with recurrent sarcoma have been tested in phase II studies using reoperative surgery plus intraperitoneal chemotherapy (Table 7.9). In all four of these studies the surgery for recurrent sarcoma was designed to completely resect cancer. The treatments with intraperitoneal chemotherapy varied greatly. Berthet and colleagues, and Eroglu and colleagues, used heated intraoperative chemotherapy.^{16,17} Karakousis and colleagues, and Eilber and colleagues, used intraperitoneal chemotherapy in a delayed manner after wound healing had occurred.^{18,23} The results of the perioperative intraperitoneal chemotherapy suggested superior results when compared to the delayed intraperitoneal chemotherapy. Figure 7.17 shows the statistically significant difference

**Figure 7.16** Heated intraoperative intraperitoneal chemotherapy for sarcomatosis following cytoreduction and for patients with a high risk for microscopic residual disease.

Table 7.8 Indications for heated intraoperative intraperitoneal chemotherapy

1. Rupture or perforated sarcoma.
2. Tumor spillage.
3. Small-volume peritoneal sarcomatosis after resection of primary sarcoma and peritonectomy of sarcomatosis.
4. Small-volume local residual disease.
5. After complete cytoreduction of sarcomatosis or sarcoma recurrence.
6. Clinical trials to test adjuvant treatments.

Table 7.9 Adjuvant regional chemotherapy for abdominopelvic sarcoma: four nonrandomized series^{16-18,23}

Series	Tumor type at presentation	Chemotherapy regimen	Mean follow-up time (range)	5-year overall survival (median)	Outcomes	Recurrence (%)
Karakousis <i>et al.</i> , 28 patients	Recurrent abdominal sarcoma	Postoperative cisplatin	17 months	7%	2 NED, 26 DOD, 1 DOC	93
Sugarbaker <i>et al.</i> , 43 patients	Recurrent abdominopelvic sarcoma	Perioperative hyperthermic cisplatin and/or doxorubicin	20 months (4–84)	39%	9 NED, 23 DOD, 10 AWD, 1 DOC	74
Eilber <i>et al.</i> , 54 patients	Recurrent abdominopelvic sarcoma	Postoperative mitoxantrone	26 months (2–98)	31%	9 NED, 35 DOD, 10 AWD	83
Eroglu <i>et al.</i> , 33 patients	Primary or recurrent retroperitoneal sarcoma	Intraoperative hyperthermic abdominal perfusion, cisplatin and doxorubicin	57 months (28–95)	49% (58 months)	15 NED, 15 DOD, 3 AWD	73

NED, no evidence of disease; DOD, dead of disease; AWD, alive with disease; DOC, dead other causes.

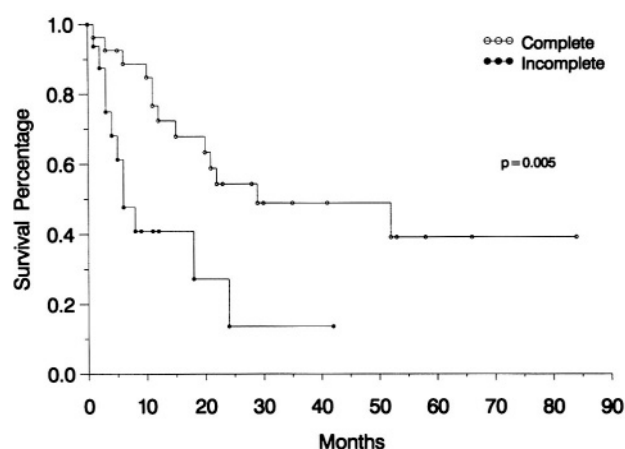


Figure 7.17 Complete versus incomplete resection of recurrent sarcoma in patients receiving perioperative intraperitoneal chemotherapy. From Berthet B, Sugarbaker TA, Chang D, Sugarbaker PH. Quantitative methodologies for selection of patients with recurrent abdominopelvic sarcoma for treatment. *Eur J Cancer*. 1999;35:413–19.

which complete resection plus perioperative intraperitoneal chemotherapy shows when compared to incomplete resection.¹⁶ Additional aggressive treatment modalities are indicated in recurrent abdominal and pelvic sarcoma along with phase III adjuvant studies in patients with primary sarcoma.

Surgical Use of Radiotherapy

Intraoperative radiotherapy has been suggested for use in patients who have positive margins of excision on bone or on other vital structures such as aorta or vena cava. Interstitial radiation therapy (brachytherapy) may be considered in some instances. However, the use of brachytherapy and intraoperative radiation therapy remains controversial, and they have not been shown to be of benefit. Unfortunately, these radiotherapy technologies have been limited to only a few centers, and no phase III data are available by which to critically evaluate these treatment options.

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8

Management of Truncal Sarcoma

Paul Sugarbaker

OVERVIEW

Sarcomas of the head, neck, trunk and breast are biologically similar to, and behave like, the soft-tissue tumors found in other anatomic areas. In the past, and now in the present, radical surgical resection with negative margins is the only reliable treatment for these sarcomas. The opportunity to use chemotherapy, surgery, and radiation therapy in selected patients as a multimodality approach may improve the likelihood of local control and long-term disease-free survival. Added experience with radiologic evaluation of patients to accurately define the anatomic location of the tumor, more definitive pathology to assess the biological aggressiveness of the lesion, and more conservative wide excisions has allowed patients to retain function and cosmesis. In addition, the development of reconstructive surgical techniques has made it feasible to reconstruct large surgical defects.

GENERAL CONSIDERATIONS

Soft-tissue sarcomas are relatively rare in the head and neck. They account for 4–15% of all soft-tissue sarcomas and less than 10% of all neoplasms at this site.^{1,2} However, it is necessary to consider sarcoma in the differential diagnosis in order to avoid serious errors in treatment. Histologic classification, tumor size and tumor grade are the major prognostic factors related to local control and survival.^{3–4} In addition, distant disease, most commonly to the lungs, is greatly influenced by these major prognostic factors.

Truncal sarcomas (chest and abdominal wall sarcomas) are also uncommon, accounting for about 20% of the soft-tissue sarcomas.^{5–7} The histologic subtype has less prognostic significance, for wide local resections with negative margins are more likely to be achieved. Special reconstruction techniques may often be required. Extensive chest wall and abdominal wall resections can be performed with low morbidity and mortality.^{3,4} Specialized radiotherapy techniques may be required to treat inadequate margins of resection. These cancers have a high local recurrence rate and local disease control is the major goal of therapy.⁶

Metastatic malignancy must always be considered in dealing with soft-tissue masses of the trunk since metastatic disease occurs with about the same frequency as do primary tumors. With truncal sarcoma there is a predominance of soft-tissue tumors over the less frequent chest wall bone sarcomas.

Breast sarcomas account for only 1% of breast malignancies. Treatment requirements are a wide excision with generous negative margins of resection. Inability to achieve a negative margin of excision carries an extremely guarded prognosis.^{8,9}

CLINICAL FEATURES AND DIAGNOSIS OF HEAD, NECK, TRUNK AND BREAST SARCOMAS

A painless mass is the initial symptom for a great majority of head and neck, trunk and breast sarcomas.¹ Other clinical signs and symptoms produced by sarcomas are related to invasion or pressure effect that the tumor exerts on the structures in these locations. The awareness of the physician that any soft-tissue mass may be a sarcoma is the most important factor in prompt diagnosis.¹ This must always be confirmed by an appropriate biopsy.

A history of prior irradiation or hereditary syndromes (Von Recklinghausen's disease, Gardner's syndrome) must be considered (Table 8.1). When dealing with a sarcoma a thorough physical and neurological examination should be performed. Plain films may be very useful prior to biopsy.

Table 8.1 Conditions related to an increased sarcoma incidence

Carcinogenic agents
Phenoxyacidic acid
Chlorophenols
Polyvinyl chloride
Thorotrast
Arsenic
Radiation therapy
Hereditary syndromes
Li–Fraumeni syndrome
Retinoblastoma
von Recklinghausen's disease
Gardner's syndrome

In performing the biopsy the surgeon must avoid several pitfalls. The skin incision or "true cut needle" tract must not jeopardize subsequent skin flaps. Hematoma must be avoided for it may propel sarcoma cells with red blood cells into and along soft-tissue planes. With these constraints in mind the biopsy must be adequate for pathological study. Necrotic tissue, hematoma or inflammatory tissue may be submitted rather than tumor tissue. A frozen section to confirm that cancerous tissue has been obtained with the biopsy may be helpful if the tissue specimen seems inadequate.

If biopsy reveals a sarcoma, plain radiographs of the anatomic site are often helpful in defining the extent of disease. Computerized tomography (CT) and frequently magnetic resonance imaging (MRI) are available for finer delineation of the tumor and to assess the extent of its local involvement. Angiography is of value in selected cases. A computerized tomogram of the chest is necessary to look for metastatic disease.

Resectability should not be based exclusively on the radiologic findings. On many occasions the only way to assess the extent of the sarcoma is by a surgical exploration to determine resectability.

HEAD AND NECK SARCOMAS

The head and neck sarcomas include a wide variety of histologic types of malignancy. Generous biopsy and accurate anatomic localization by CT are necessary prior to surgical intervention, radiotherapy and/or chemotherapy.

Histopathologic Types of Head and Neck Sarcomas

Aggressive Fibrous Lesions

These are neoplasms that arise from cells of the fascia or fibroblasts. The aggressive fibrous lesions include aggressive fibromatosis, dermatofibrosarcoma protuberans, fibrous histiocytoma and desmoid tumors. Although these locally malignant diseases present a broad spectrum of invasive capabilities, they are usually nonmetastasizing lesions. Fibrosarcoma, however, differentiated or undifferentiated, implies the potential for metastasis. Because many of these lesions are slowly progressive, and seldom if ever metastasize, some authors do not consider desmoid tumors and dermatofibrosarcoma protuberans as true sarcomas. Others consider aggressive fibromatosis as low-grade fibrosarcomas. Patients with low-grade fibrosarcomas or dermatofibrosarcoma protuberans have a longer survival than patients with higher-grade tumors, but may eventually succumb to cancer or require major amputation though metastatic potential is very low. Surgical resection is the treatment of choice. Adjuvant radiation therapy may play a role in order to obtain local control when positive margins of resection are left behind. Devastating problems may arise when these sarcomas progress along the brachial plexus into the cervical neural foramina.

Malignant Fibrous Histiocytoma (MFH)

These are often aggressive lesions with a poor prognosis in spite of multimodal treatment. They can occur within the treatment field of previous radiotherapy for other disorders. Adjuvant treatment is of limited value but worthy of consideration in selected patients. These tumors – along with fibrosarcomas, aggressive fibromatosis, and dermatofibrosarcoma protuberans – account for about 50% of head and neck sarcomas.¹

Adult Rhabdomyosarcoma

This sarcoma of skeletal muscle lineage is the most common malignant soft-tissue tumor of the head and neck in children, the orbit being a very frequent location. Rhabdomyosarcoma in adults is usually located in the pterygoid region. Prognosis is worse in adults as compared to children because the adult rhabdomyosarcoma is much less responsive to chemotherapy and to radiotherapy. Adult rhabdomyosarcoma tends to be locally invasive, spread along tissue planes, and metastasize hematogenously and lymphatically early in its course. Adult rhabdomyosarcoma is unique among soft-tissue sarcomas in that lymphatic metastases are present in up to 50% of cases. Radiation therapy and

chemotherapy play a major role in treatment, and surgery is often used only for diagnosis purposes. Occasionally surgery may be used to resect persistent tumor after maximal chemotherapy or chemoradiation therapy has been employed. The margins on these operations employing "consolidation surgery" are usually minimal or absent. Surgical resection is the initial treatment option for rhabdomyosarcomas if negative margins of resection can be achieved.

Leiomyosarcoma

The sarcomas of smooth muscle lineage are relatively common in the head and neck. They arise from cells of blood vessels or from an undifferentiated mesenchymal cell. Surgical resection is the treatment option and the recurrence rate is as high as 75%.

Hemangiopericytoma

This is a rare neoplasm of capillaries and the pericytes around and between the blood vessels. Children have a better outcome, and an adverse prognosis increases with age. Local recurrence rate is about 40% but this tumor results in distant metastasis in only about 10% of patients. Clinical outcome is closely related to the site of origin because this will usually determine the adequacy of the margins of resection. Treatment is surgical resection if feasible.

Angiosarcoma

This is an uncommon tumor in the head and neck, with the scalp being the most frequent site. It is more commonly seen in older patients. Lymph node metastases are present in 25–50% of cases. A characteristic feature of this neoplasm is its clinically undetectable diffuse infiltration far beyond the visible limits of the primary lesion. Prognosis is poor and surgical resection along with radiation therapy and chemotherapy are usually the options for management.¹

Neurofibrosarcoma

These tumors arise from Schwann cells; this histologic type occurs as a sarcomatous degeneration of a neurofibroma in patients with Von Recklinghausen's disease. Clinical signs and symptoms may occur within the distribution of the large nerve that is involved. Superficial lesions have a better prognosis than deeper ones. These tumors are frequently locally recurrent, and when hematogenous spread occurs are uniformly fatal. Wide surgical excision and radiation therapy for inadequate margins of resection are the treatment options of choice.

Liposarcoma

This is also a rare neoplasm in the head and neck. This sarcoma arises from lipoblast cells and not from pre-existing lipomas. Although the well-differentiated liposarcoma of the neck has a good prognosis, tumors arising in the oral cavity or the oropharynx have a poor outcome. The incidence of local recurrence is high unless complete resection is achieved. Surgical excision with negative margins of resection is by far the best approach if this can be achieved.

Other rare sarcomas in the head and neck region include synovial sarcoma, alveolar soft-part sarcoma, and chondrosarcomas (Table 8.2).

CLINICAL FEATURES AND DIAGNOSIS OF CHEST WALL AND TRUNCAL TUMORS

Malignant chest wall tumors comprise approximately 50% of all primary tumors at this location. Malignant tumors are more likely to produce overt signs and symptoms (painful enlarging mass) than are benign neoplasms.^{3,7,8} Accurate and early diagnosis is the first step in successful management of any primary chest wall tumor, since types of treatment vary for each malignancy. These tumors are seen in males twice as frequently as in females. An accurate clinical history of prior radiotherapy or a hereditary syndrome, a physical examination along with a proper biopsy, remain the standard methods for diagnosis.

Histopathologic Types of Chest Wall and Truncal Sarcomas

Histologic types are similar to those more commonly seen in the extremity. Fibrosarcoma and malignant fibrous histiocytoma are the most frequent soft-tissue sarcoma in this location and chondrosarcoma is the most common chest wall bone sarcoma.

Table 8.2 Histologic types of sarcomas of the head and neck

Fibrosarcoma	Synovial cell
Malignant schwannoma	Angiosarcoma
Dermatofibrosarcoma protuberans	Hemangiopericytoma
Aggressive fibromatosis	Rhabdomyosarcoma
Malignant fibrous histiocytoma	Leiomyosarcoma
Liposarcoma	Neurofibrosarcoma

Chondrosarcomas

Chondrosarcoma is the second most common tumor of bone after osteogenic sarcoma, and comprises about 20% of all primary bone tumors. Chondrosarcoma usually appears in middle-aged or older adults. The pelvic girdle (27%), chest wall (ribs and sternum (15–20%)), femur (23%), and humerus–scapula (16%) are the most frequent sites of origin. These sarcomas arising from cells of cartilage lineage are one of the most common primary malignant tumors of the chest wall. Costochondral junction and sternum are the frequent locations.

Chondrosarcomas may be of primary (65%) or secondary (35%) origin, depending on whether they arise *de novo* or from a pre-existent benign cartilage tumor. Repeat surgical resections for tumor recurrences usually precede malignant transformation. Chondrosarcomas may also be induced by previous irradiation (9%).

Clinical presentation is usually as a slow-growing painful mass, and presence of symptoms is generally of value to differentiate these tumors from their benign counterparts. Pain also has a role to discriminate chondroma from chondrosarcoma of the chest wall.¹⁰ Radiologic findings may show soft-tissue involvement and bone destruction. Multiple radiologic features have been described, but probably the presence of irregular calcifications throughout areas of radiolucency with trabeculation, and the presence of the Codman's triangle (long bones) are the most significant radiologic signs. CT and MRI are excellent tools for an accurate and complete anatomic staging. Angiography is useful if vascular involvement is in question.¹⁰

Guidelines for Management and Treatment Options for Chondrosarcomas

A special problem in management arises in caring for patients with chondrosarcomas. These lesions have a great heterogeneity in terms of grade of malignancy in different parts of the primary tumor mass. Frequently a biopsy from one portion of the sarcoma will show a well-differentiated lesion suggesting a good prognosis and no need for wide margins of excision. Another area may be widely undifferentiated; of course the prognosis and selection of treatment options is determined by the most aggressive histology that is seen.

Because of this prominent heterogeneity a unique management plan is recommended for both extremity and truncal chondrosarcoma. After a radiologic diagnosis is made the entire tumor is curetted from its normal bone and soft-tissue margins. Liquid nitrogen is used to treat the cavity and extend the margins. Bone chips are used to loosely fill the empty space. Free margins of excision that would be achieved by a

resection are not attempted. If a low-grade I or IIa tumor is diagnosed by a complete histopathologic searching of the specimen, no further treatment is required. If a grade IIb or grade III focus of chondrosarcoma is found then a definitive resection with generous negative margins of excision are required. The prognosis with grade III lesions, mesenchymal chondrosarcoma, and clear-cell chondrosarcoma is guarded.

Plasmocytoma

This is a relatively frequent neoplasm since 25–30% of all primary malignant tumors in the chest wall are of this type (solitary plasmocytoma). Signs and symptoms of a generalized disease such as fever, weakness and anemia may be present since myeloma is also a systemic disease. Increased serum proteins are a common finding. Surgery must be used only for diagnosis purposes. Systemic chemotherapy is the treatment option of choice. Radiation therapy is useful for symptomatic pain relief.

Osteogenic Sarcoma

Typically osteosarcoma of the chest wall is a rapidly growing malignancy of the pediatric patient. Osteosarcoma that occurs in the chest wall presents a poor prognosis (20% 5-year survival). Pulmonary metastases occur early in the course of the disease. Chest wall osteosarcoma usually presents as a painful expanding mass and the characteristic radiological appearance is "sunburst-like." Wide local en-bloc resection is the treatment of choice after aggressive systemic chemotherapy has caused maximal shrinkage of the primary tumor. The prognosis remains very poor but is undoubtedly improved when there is an objective response to chemotherapy.

Ewing's Sarcoma

This neoplasm is usually seen in the pediatric patient. Although it usually arises in long bones, the chest wall (ribs) can also be affected.⁸

Desmoid Tumors

These are rare neoplasms in the chest wall and some authors consider them as benign tumors while others consider them as low-grade fibrosarcomas because of the aggressive local fibrosis they show. Women are more commonly affected. Recurrence rate is very high if complete resection is not achieved. Wide resection is the treatment option for primary and recurrent disease.

Giant-cell Tumors of Bone

Giant-cell tumor of bone is a non-metastasizing lesion that is locally aggressive. If inadequately treated it may recur and eventuate in a fully malignant sarcoma with definite metastatic potential. Giant-cell tumor of bone is histopathologically well characterized by multinucleated giant cells uniformly dispersed throughout a well-vascularized tissue made up of plump, spindle or ovoid cells. It represents about 5% of all primary bone tumors. These tumors are more common in the third and fourth decades of life and women are slightly more affected than men. Secondary aneurysmal bone cyst arising in a giant-cell tumor of bone has been confirmed.¹¹

More than 75% of giant-cell tumors are located around the articular end of a long tubular bone. Giant-cell tumors of the sacrum are second in incidence to chordoma at this site. Vertebral giant-cell tumors are uncommon but may occur. Multiple giant-cell tumors of bone that appear at different sites in the same patients are rarely seen. Malignant transformation may occur after multiple or even solitary local recurrence of a previously benign giant-cell tumor. A malignant sarcomatous growth will occur at the site of a previously documented benign giant-cell tumor in approximately 5% of patients. These sarcomatous changes usually occur after radiation therapy of a previous benign lesion and are considered to be radiation-induced malignancies. Fibrosarcoma, malignant fibrous histiocytoma, and osteogenic sarcoma are the most common lesions.

A primary malignant giant-cell tumor of bone may occur in 2% of these lesions. It is defined as a newly diagnosed sarcoma in which a histologically identifiable benign giant-cell tumor component is present. The sarcomatous component is usually a malignant fibrous histiocytoma or fibrosarcoma.

Physical findings relate to the involved bone and are nonspecific. They include pain, swelling, tenderness, and limited motion. Tumors located in the spine and sacrum often present with neurologic disturbances.

Radiologic studies reveal lesions arising in the axial skeleton that appear as ill-defined lytic areas lacking specific radiographic features. Sacral lesions even of considerable size may not be recognized as giant-cell tumors because of lack of consistent features. The radiographic appearance of giant-cell tumors cannot differentiate between benign and malignant forms. The angiographic assessment of giant-cell tumors reveals marked tumor vascularity. Size, extent of the lesion, and soft-tissue involvement can be evaluated from an angiogram. Contrast-enhanced CT is a useful noninvasive diagnostic method. Giant-cell tumors involving the bony pelvis are well defined by CT scan, especially if intrarectal air and contrast are used. MRI correctly

defines the size and extent of soft-tissue extension but rarely adds information to the CT findings. Radionuclide bone scanning of giant-cell tumor of bone is of limited diagnostic value.

Treatment of tumors in the sacrum or vertebral bodies is difficult because the lesions are advanced at the time of diagnosis and are less accessible for total removal. Radiotherapy is often required for better management and local control. Total sacrectomy by piecemeal excision of tumor from around nerve roots and/or radiotherapy may provide a long-term cure of tumors at this location. Complete removal is the treatment option of choice when feasible for giant-cell tumors of the pelvis, sacrum, or spine. Curettage or local excision is often all that is possible surgically using radiotherapy for incomplete removal, recurrence or nonresectability. Vertebral giant-cell tumors are more common in the lumbar region. Extensive intralesional excision and arthrodesis with or without radiotherapy achieves the best results. Marginal en-bloc excision is advised only for well-defined lesions not involving the posterior arch or soft tissues. Autogenous bone grafting may be necessary to fill the surgical defects. Curettage and cryosurgery are alternative therapies in some cases.¹¹

These tumors show a high local recurrence rate of approximately 30% within the first 2 years and about 50% in 5 years when the Curettage approach is employed. About 20% of giant-cell tumors, even in the total absence of histologic malignancy, invade the cortex and directly extend into adjacent soft tissues.

Other malignant tumors which may be present in the chest wall include: fibrosarcoma, angiosarcoma, rhabdomyosarcoma, neurosarcoma, and liposarcoma (Table 8.3).

Histopathologic Types of Abdominal Wall Sarcomas

Two histologic groups are the most frequent tumors of the abdominal wall. Desmoid tumors (low-grade nonmetastasizing fibrosarcomas) and fully malignant soft-tissue sarcomas (rhabdomyosarcoma, fibrosar-

coma, leiomyosarcoma, liposarcoma, synovial sarcoma, malignant fibrous histiocytoma, etc.) with malignant potential for metastasis.

Desmoid Tumors of the Abdominal Wall

Desmoid tumors often recur after inadequate resection. These are usually slow-growing tumors with no tendency for metastatic spread, although they can cause death from local effects. Prognosis is good and long-term survival is the normal outcome. Wide resection is the optional treatment.

Fully Malignant Soft-tissue Sarcomas of the Abdominal Wall

These rapidly growing tumors recur and metastasize with great frequency. Prognosis is poor, as well as long-term survival. Wide en-bloc resection including full-thickness abdominal wall when deeply located is the option of choice. Adjuvant chemotherapy is advisable to prevent distant disease but definitive studies in this regard are not available.

Histopathologic Types of Breast Sarcomas

Mammary sarcomas are malignant neoplasms of the breast which arise from mesenchymal tissues.⁹ They comprise a wide range of tumors including lymphomas, cystosarcoma phyllodes, and the entire spectrum of connective tissue tumors. The most common histologic types are malignant fibrous histiocytoma, fibrosarcoma, and liposarcoma. Angiosarcoma occurs disproportionately more often in the breast than at other sites in the body. The term stromal sarcoma describes the group of mammary sarcomas other than lymphoma, angiosarcoma, and malignant cystosarcoma. However, this term should be used for lesions that arise from the specialized stroma of the breast. Intermediate and high-grade sarcomas constitute the majority of breast sarcomas and are certainly capable of metastasizing systemically.⁹

PROGNOSIS OF HEAD AND NECK, TRUNK AND BREAST SARCOMAS

The most important prognostic factors affecting survival are discussed below. Estimates of survival are presented in Tables 8.4 and 8.5.

Histologic type

Differences in survival can be attributed to the variable local behavior and metastatic potential of the different histologic types. However, each histologic type of sarcoma presents a wide range of aggressiveness for

Table 8.3 Histologic types of soft-tissue and bone sarcomas of the chest wall

Fibrosarcoma	Ewing's sarcoma
Malignant fibrous histiocytoma	Osteogenic sarcoma
Chondrosarcoma	Hemangiosarcoma
Rhabdomyosarcoma	Plasmocytoma
Liposarcoma	Leiomyosarcoma
Neurofibromatosis	Desmoid tumors

Table 8.4 Long-term survival of head and neck sarcomas

Study	Year	5-year OS (%)	10-year OS (%)
Figueiredo <i>et al.</i>	1987	38	32
Farr <i>et al.</i>	1981	32	–
Freedman <i>et al.</i>	1989	68	60
Greager <i>et al.</i>	1984	54	28
Weber <i>et al.</i>	1986	40	30

Table 8.5 Long-term survival of chest wall sarcomas

Study	Year	5-year OS (%)	10-year OS (%)
Gordon <i>et al.</i>	1990	66	56
Greager <i>et al.</i>	1987	51	34
Perry <i>et al.</i>	1989	65*	59†
Paerolero <i>et al.</i>	1985	57	49

* 3-year survival.
† more than 5 years.

local invasion and distant metastasis. For this reason each of these soft-part and bone tumors must be considered individually. Prognosis is assessed through the sarcoma grade for that particular histologic type.

Histologic Grade

Differentiation grade (low- vs. high-grade) also correlates with survival and determines to a large extent local control and distant metastasis. The pathologist considers necrosis as the most reliable histologic finding by which to determine grade. Other considerations are mitotic activity and nuclear atypia.

Tumor Size

Tumors equal or larger than 5 cm usually have a poor prognosis; in contrast, tumors smaller than 5 cm have a better outcome. Size will be of great significance for head and neck sarcomas whereas tumor size for chest wall sarcomas does not seem to be such a strong prognostic determinant.

Response to systemic chemotherapy may vary with tumor size.

Margin Status

The adequacy of the surgical resection is an important prognostic factor. Selecting an adequate margin of resection for a lesion with a particular biological

aggressiveness without unnecessary sacrifice of function is a most difficult but necessary task. Positive surgical margins regardless of adjuvant therapies constitute the single greatest factor leading to local recurrence. The facility of performing a satisfactory wide excision is obviously dependent on tumor location.¹ Margin status affects both disease-free survival and overall survival. Liquid nitrogen has been used to improve the margin of resection on low-grade bone tumors, with excellent results. Low-grade chondrosarcoma and giant-cell tumors are commonly treated in this manner. Radiation therapy has traditionally been the treatment option to reduce the likelihood of local recurrence with narrow margins of resection

Metastasis

Presence of metastasis has a significant adverse effect on survival. Metastasis is by far most common to the lungs except for visceral sarcoma where the first capillary bed draining the primary tumor is the liver.

Prognosis Regarding Breast Sarcoma

Adverse prognostic factors for breast sarcomas include high histologic grade, and high mitotic rate. Tumor size seems not so important to outcome. Breast sarcomas are usually detected earlier than tumors at other sites with a median size of 4 cm.

TREATMENT OPTIONS FOR HEAD AND NECK, TRUNK AND BREAST SARCOMAS

Wide local en-bloc resection with adequate margins is the treatment of choice. This usually results in local control. A high rate of local recurrence is to be expected if wide excision is not sought or cannot be achieved. Low-grade tumors do not usually require adjuvant therapies.

Lymphadenectomy is not routinely performed unless nodes are clinically involved. Nodal involvement and distant spread is most commonly seen in high-grade tumors.

Adjuvant treatment with both radiotherapy and chemotherapy are often recommended in selected patients in an attempt to achieve local control and prevent distant disease. Indications are microscopic or gross positive margins of resection and narrow margins with large high-grade tumors.

Treatment Options for Head and Neck Sarcomas

Cosmetic and functional results are important in head and neck sarcomas and microscopic disease can often

be controlled with radiotherapy, avoiding a radical resection. The role of adjuvant radiation therapy is to sterilize microscopic extensions beyond the resection margins. Radiotherapy improves local control and survival over results achievable with surgery alone.

Chemotherapy is not effective as a single-modality treatment but may help control micrometastatic disease in the lungs and augment the local control provided by radiation therapy. Unfortunately, even aggressive multimodality therapy may fail to control primary disease. Local control and distant metastasis remain a therapeutic challenge for improving survival in high-grade tumors.¹

Treatment Options for Chest Wall Sarcomas

En-bloc surgical resection with negative margins by using strict surgical oncologic techniques continues to be the most fundamental treatment of most tumors of the chest wall.⁸ This is usually effective for local control in low-grade tumors.

The surgical resection of major chest wall tumors requires special preoperative planning with consideration of the overall condition of the patient, the status of the overlying skin, the anticipated skeletal defect and the available options with respect to reconstruction and support.⁸ With appropriate preoperative attention to skin and soft-tissue coverage plus skeletal support, resection and reconstruction of major chest wall tumors can be accomplished. Reconstructive techniques available to deal with the resulting defects are presented below.⁵ Full-thickness resection of the chest wall is advised for all high-grade sarcomas. Previous biopsy sites must be included. An aggressive surgical approach

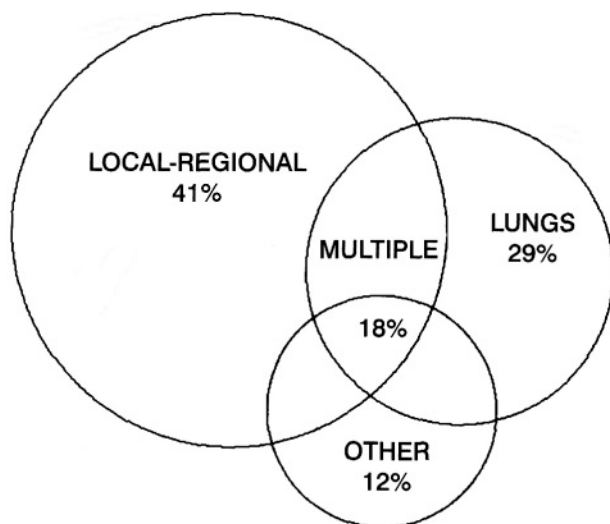


Figure 8.1 Truncal sarcomas. Patterns of recurrence.

also applies for recurrences since local relapse and pulmonary metastases remain the most common sites of treatment failure⁴⁻⁶ (Figure 8.1).

Adjuvant radiation therapy and chemotherapy are selectively used for high-grade sarcomas. They are routinely employed for residual disease and positive or equivocal margins of resection in an attempt to gain local control and prevent distant disease.⁴ Innovative multimodal techniques for induction chemotherapy and perioperative radiotherapy are needed to optimize modern sarcoma management (Figure 8.2). However, it must be emphasized that adjuvant chemotherapy and radiotherapy has been used in randomized and nonrandomized studies for patients with high-grade sarcomas, with disappointing results.¹²⁻¹⁴ For truncal sarcomas chemotherapy seems to improve disease-free survival.¹³ Radiotherapy is mainly used for local control, although benefits similar to those seen with extremity sarcoma have not been reported. More clinical research is required to improve survival, and to better define the precise indications for use of chemotherapy and radiotherapy for head and neck, truncal and breast sarcomas. Elective lymphadenectomy is not

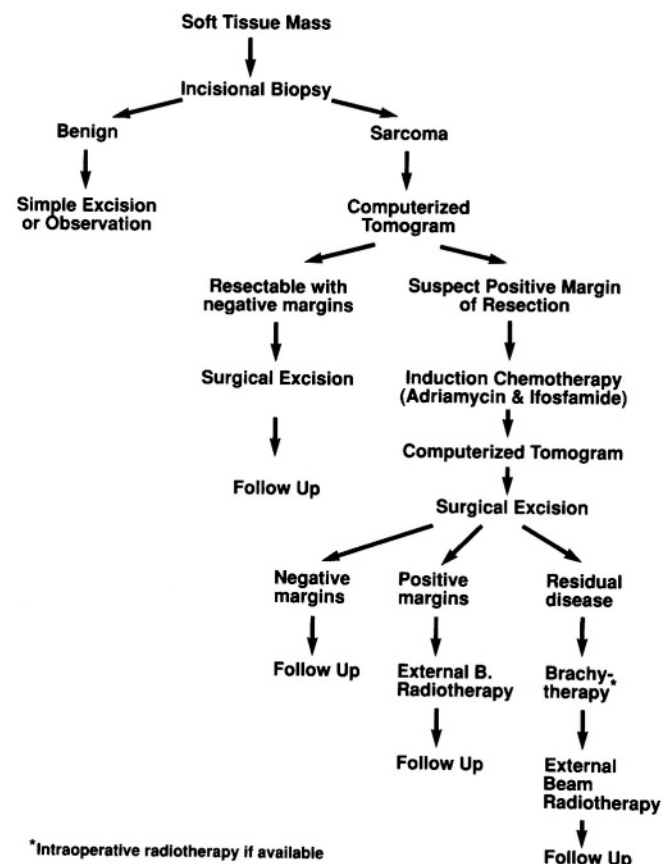


Figure 8.2 Clinical pathway for management of head and neck, trunk, and breast sarcomas.

routinely performed. However, it should be considered in certain high-grade types such as rhabdomyosarcomas, synovial cell sarcoma, and epithelioid sarcoma if these malignancies are immediately adjacent to the axillary nodes. Inguinal nodes are spared to avoid lower-extremity edema.

Treatment Options for Breast Sarcomas

Breast sarcoma is recognized as a separate entity from the more common breast carcinoma, and differences in the behavior of the two tumors must be kept in mind when planning treatment. The strategy used must be based on the knowledge of the biologic behavior of the tumor, including its pathways of spread. Contemporary multimodal approaches include excision of the soft-tissue sarcoma with adjuvant radiation and chemotherapy. However, excellent local control is possible with mastectomy alone if adequate margins are achieved.⁹ The failure to establish local control is associated with poor prognosis. Axillary lymphadenectomy is indicated only when tumor is palpable within the nodes or when technically necessary to achieve local control of the primary tumor. It must be emphasized that surgery remains the most important treatment option for most mammary sarcomas. Some sarcomas require simple mastectomy for adequate treatment while others may need only wide local excision. If simple mastectomy does not provide sufficient clearance one must pursue radical mastectomy in order to obtain local control.⁹

Adjuvant therapy with estrogen antagonists, and other hormone manipulations, currently have no place in the treatment since these tumors do not appear to display hormone receptors.

General Guidelines for Wide Excision of Head, Neck, Trunk and Breast Sarcoma

The steps required to complete the surgical resection of a head and neck, truncal and breast sarcoma are as follows:

1. Obtain and display in the operating theater a CT of the lesion and of the lungs to help determine operability for cure and the anatomic site(s) that will be the least margin of dissection. If magnetic resonance images or angiograms were required, they must also be visible to the surgeon during the progress of the dissection.
2. Excise the skin approximately 1 cm around the biopsy site and dissect skin flaps back to the furthest extent of the palpable lesion.
3. Determine as early in the operation as is possible whether the patient is resectable for cure. If the patient is found by surgical exploration to be

inoperable for cure (gross residual disease) minimize the quality-of-life sacrifices and the cost that will result from the treatment.

4. Be prepared to use intraoperative radiotherapy or brachytherapy to definitively treat small areas of gross residual disease.
5. Avoid removal of lymph node groups (axillary or inguinal) surrounding the sarcoma mass unless they are encompassed by the dissection or are palpably involved by tumor.
6. Use electrosurgical dissection with complete muscle relaxation to divide muscle and fascia 1–2 cm beyond the palpable extent of the tumor. Repeatedly assess the adequacy of the margins during the dissection. Avoid resection of entire muscle bundles unless they are directly adjacent to tumor.
7. Tag with sutures divided muscles, tendons, or fascia that may be used in soft-tissue coverage, stabilization or reconstruction.
8. Dissect the least margin of resection by electro-evaporation using ball-tip electrosurgery and a smoke evacuator. This will minimize the spill of sarcoma tumor emboli and gain a 1–2 mm margin as a result of heat necrosis.
9. If a spill of sarcoma tumor emboli into the operative field occurs irrigate copiously with a 1% peroxide. If the sarcoma dissemination occurred within the pleural or peritoneal cavity use intracavitary chemotherapy.¹⁵
10. Generously mark out the extent of the dissection with metal clips to facilitate radiotherapy should it be necessary.
11. Reconstruct and/or stabilize the operative site by myodesis, marlex or prolene mesh, myocutaneous flaps, autologous or allogenic fascia.
12. Meticulously close the subcutaneous tissue and skin over generous closed-suction drainage.
13. Obtain a CT of the operative site approximately 1 month after surgery to use as a baseline examination that documents postoperative changes.

TECHNICAL ASPECTS OF RECONSTRUCTION

The operative management of massive chest or abdominal wall malignancies presents an infrequent but formidable surgical challenge. Massive chest or abdominal wall resection for malignancy must be pursued aggressively whenever these lesions are encountered. Designing a surgical strategy which provides adequate margins and immediate reconstruction is critically important. The age of the patients and the locations or size of the lesions are not significant factors. These operations can be performed safely, and the benefits to patients justify this extensive surgery.

The use of muscle pedicle flaps has greatly enhanced the surgeon's ability to deal with large chest or abdominal wall defects. Pectoralis major or latissimus dorsi muscles, for instance, are equally effective in providing full-thickness coverage.^{16,17} The surgical axiom that stabilization of the chest is mandatory before closure may not be infallible. A plastic mesh is appropriate in many instances. However, defects can often be closed depending on size and location, by moving in appropriate muscle flaps, without the use of synthetic material or natural tissues (fascia lata). Most patients will not show evidence of pulmonary compromise and prosthetic material will be obviated.

Prosthetic Materials

When a patient requires full-thickness chest or abdominal wall resection for malignant tumors, careful preoperative planning is crucial, not only to ensure a negative margin, but also in the production of a physiologically and cosmetically acceptable reconstruction at the conclusion of the procedure.⁸ Chest and abdominal wall immediate reconstruction sometimes requires the use of synthetic prosthetic devices to cover large defects in order to preserve physiologic functions and prevent paradox. Where no musculofascial or musculo-cutaneous flaps are available, or when considered inappropriate or unnecessary, a different sort of autogenous tissue (omentum, fascia lata), meshes, or other inert material (methyl methacrylate) can be used as long as full-thickness skin cover is assured. Crucial to the use of any synthetic material is that it must be placed under tension when sewn into place.⁸ Infection, prior radiation therapy, need of postoperative radiotherapy or chemotherapy, and foreign-body intolerance must be taken into account when considering these reconstruction techniques. Marlex mesh, Prolene mesh, Gore-Tex sheets, and methyl methacrylate are examples of prosthetic materials available for use in individualized situations.

Myocutaneous Flaps Commonly Used for Head and Neck, Chest or Abdominal Wall Reconstruction after Wide Resections for Tumors

1. *Sternocleidomastoid flap.* This is an excellent flap for the middle aspect of the face or the lower face. It is frequently used for intraoral and pharyngeal lining as well as a potential bone graft (along with clavicle) for mandibular reconstruction. It has also been employed to reconstruct the orbit.
2. *Pectoralis major flap.* This is probably the most commonly used flap in head and neck reconstruction and is usually employed for external resurfacing

of skin at these sites, coverage of orbital defects, intraoral and pharyngeal lining, and as a carrier for rib and skin in mandibular repair. Reconstruction of the esophagus has also been done. In addition, transposed pectoralis major muscle has been employed for closure of chest wall defects. Single or bilateral pectoralis major muscle flaps with skin grafts are particularly useful for coverage of large anterior chest wall defects (Figure 8.3).

3. *Latissimus dorsi flap.* This versatile flap can be used in head and neck reconstruction for defects of the posterior neck and shoulder as well as intraoral and pharyngeal repair. The latissimus dorsi flap is particularly suited for use in closure of large midline trunk defects (front and back) and especially for breast reconstruction after mastectomy. Latissimus dorsi will also reach and cover the upper abdomen just below the costal margin, and lateral abdominal wall. However, this flap is of limited use for abdominal wall reconstruction (Figure 8.4).
4. *Trapezius flap.* This is a less widely used flap than pectoralis major flap for head and neck reconstruction; it is commonly used as a secondary option in patients in whom pectoralis major muscle flaps have failed to provide adequate coverage. The trapezius muscle flap has also been used to close upper anterior or posterior chest wall defects.

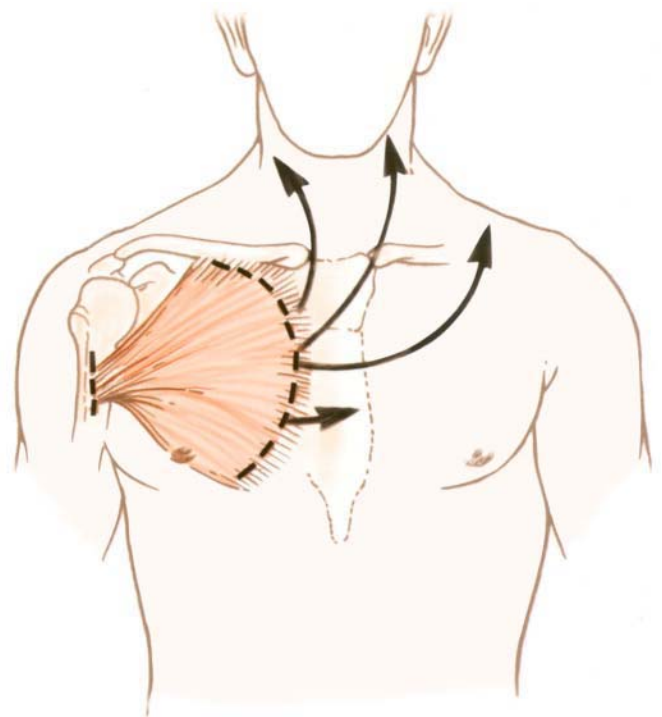


Figure 8.3 Pectoralis major musculocutaneous flap.

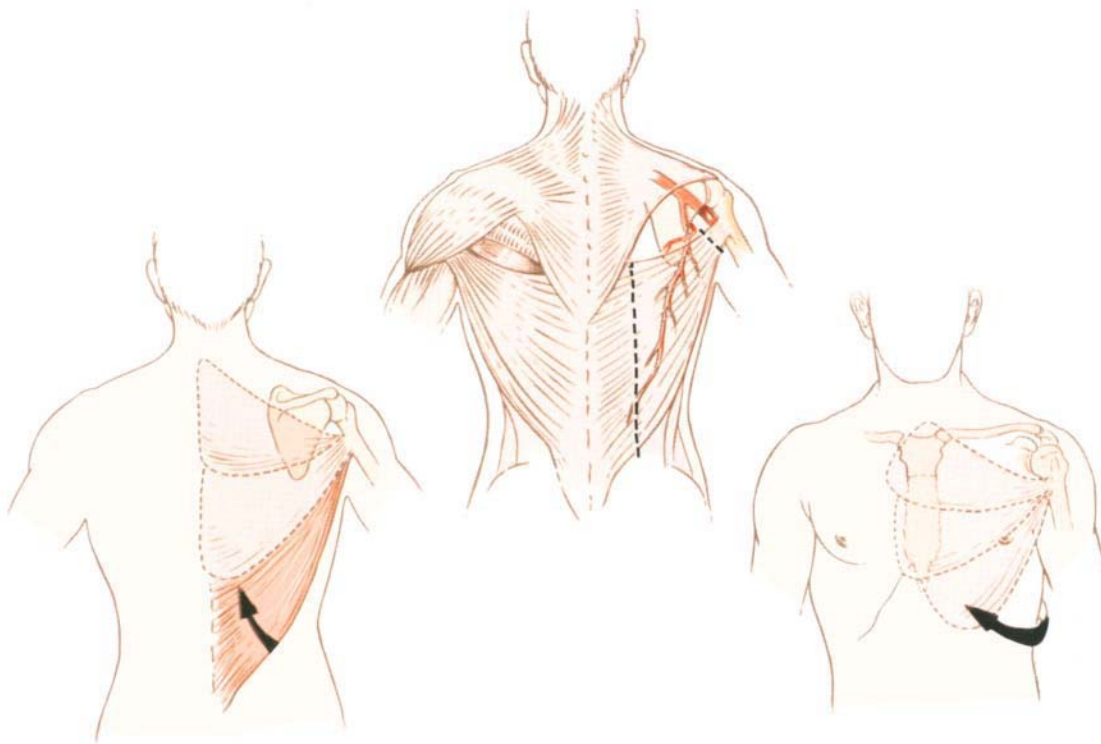


Figure 8.4 Latissimus dorsi musculocutaneous flap.

5. *External oblique flap.* The external oblique muscle flap is mainly used to cover small upper or lower full-thickness abdominal wall defects, although it is not so widely employed as the pectoralis major or latissimus dorsi flaps in chest wall reconstruction or even abdominal wall reconstruction because of its limited use. However, it can certainly provide full-thickness tissue for abdominal wall integrity and soft-tissue coverage and is also useful for correction of midline hernia defects.
6. *Tensor fascia lata flap.* Tensor fascia lata flap is one of the most useful flaps for reconstruction of abdominal wall full-thickness defects. It can be used as a musculofascial or extended musculocutaneous flap. In general, the use of tensor fascia lata flap is limited to the lower half or two-thirds of the abdominal wall. On the other hand, tensor fascia lata myocutaneous free flap is the best means of providing chest wall stability and coverage of large, potentially contaminated chest wall defects (Figure 8.5).
7. *Rectus femoris flap.* This is an excellent and reliable flap that will provide soft-tissue coverage for the abdominal wall. It can be elevated with the fascia lata to reconstruct muscular and fascial defects. It is mainly a second-choice flap if a tensor fascia lata flap is not available. The rectus femoris flap is a more muscular flap and some functional loss in the lower extremity may result after its use.
8. *Rectus abdominis and transverse rectus abdominis muscle flap.* The rectus abdominis flap is often used when considering abdominal wall reconstruction. This unit may provide skin and soft-tissue coverage but does not contribute to maintenance of abdominal wall integrity because of muscle denervation. The use of the superior half of the rectus abdominis muscle (based on the inferior epigastric artery) does not excessively weaken the abdominal wall, because of the strength of the anterior and posterior rectus sheath (Figure 8.6, left). In contrast, the use of the inferior portion of the rectus muscle (based on the superior epigastric artery) may lead to weakening of the lower abdominal wall because of the weak posterior rectus sheath (Figure 8.6, right). The transverse rectus abdominis muscle flap is an excellent flap for full-thickness chest wall defects and allows for adequate fascial reconstruction of the abdominal wall.
9. *Inferior gluteal thigh flap.* Large tumors deep in the pelvis may require extensive sacrifice of perineal skin and soft tissue. After an abdominoperineal resection, recurrence in the perineal incision may require wide

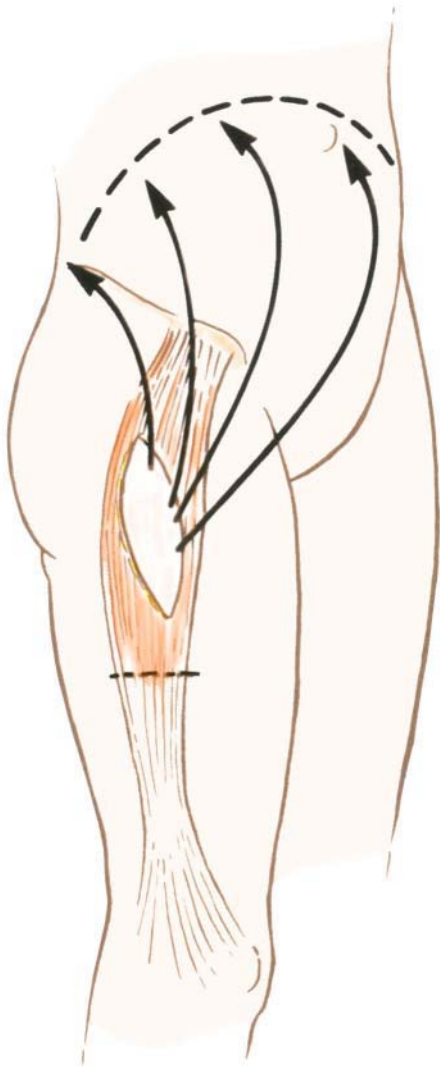


Figure 8.5 Tensor fasciae lata musculocutaneous flap.

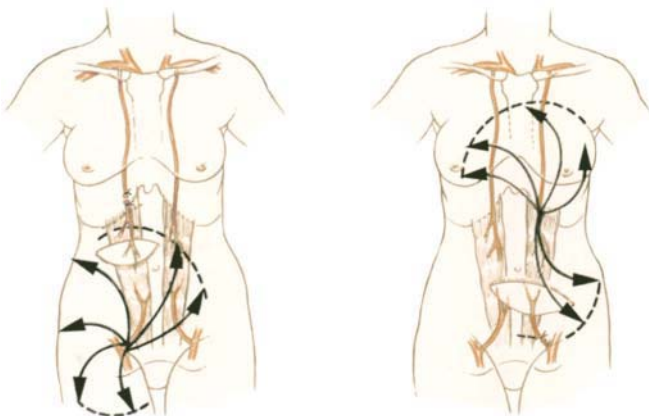


Figure 8.6 Superior (left) and inferior (right) rectus abdominis muscle flap.

re-excision. If radiation therapy was used the tissues will be immobile and failure of perineal wound healing will be common. Several techniques have been developed to transplant fresh tissue into the perineal defect to allow pelvic integrity and function to be restored. The inferior gluteal thigh flap provides a generous volume of tissue to be transferred into the perineal defect (**Figure 8.7**).

FOLLOW-UP

Patients undergoing surgical resections for head and neck, chest wall or abdominal wall sarcomas should be followed up at regular intervals during the first 5 years. All patients should be seen every 3 months for the first 2 years after surgery and at 6-month intervals up to 5 years. Complete physical examinations, blood chemical evaluations and chest X-ray films should be obtained at each visit. In addition, chest and abdominal CT must be performed every 6 months for the first 3 years. Bone scans can also be obtained in selected patients on a yearly basis.

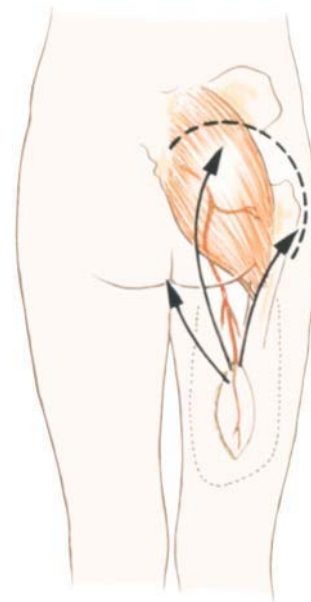


Figure 8.7 Inferior gluteal thigh flap.

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9

Overview of Resections around the Shoulder Girdle: Anatomy, Surgical Considerations and Classification

Martin Malawer and James Wittig

OVERVIEW

The Tikhoff–Linberg procedure and its modifications are limb-sparing surgical options for selected patients with bone and soft-tissue tumors in and around the shoulder girdle. Today, approximately 95% of patients with tumors of the shoulder girdle can be treated by a limb-sparing procedure. Forequarter amputations are rarely performed, except in cases of tumors that are infected or fungating, tumors that invade the adjacent neurovascular bundle or chest wall, and failed attempts at limb-sparing resections. Function of the forearm, wrist, and hand should be nearly normal following a limb-sparing shoulder girdle resection. A stable shoulder and elbow flexion and extension are achieved without the need for an orthosis.

This chapter describes in detail the specific tumor site and its influence on the surgical management, indications and contraindications of resection, surgical staging and classification, endoprosthetic reconstruction and design features, functional considerations, and rehabilitation. Specific techniques of resection and reconstruction of the proximal humerus and scapula are presented in Chapters 33 and 34.

INTRODUCTION

The upper extremity is involved by bone and soft-tissue neoplasms one-third as often as the lower extremity.¹ The scapula and proximal humerus are common sites of primary sarcoma, including osteosarcoma and Ewing's sarcoma in children and chondrosarcoma in adults.² When soft-tissue tumors occur in the upper extremity, they tend to favor the shoulder girdle. Metastatic tumors, in particular hypernephroma, also have a propensity for the proximal humerus.

The shoulder girdle consists of the proximal humerus, the scapula, and the distal third of the clavicle, as well as the surrounding soft tissues (Figure 9.1A). Each bone may be involved by a primary malignant bone tumor or metastases, with or without soft-tissue extension. The bones of the shoulder girdle may also be secondarily involved by a soft-tissue sarcoma and require similar resection and reconstruction techniques (Table 9.1).

Until the mid-twentieth century, forequarter amputation was the treatment for malignant tumors of the shoulder girdle. Today, approximately 95% of patients with sarcomas of the shoulder girdle can be treated safely by limb-sparing resection. The Tikhoff–Linberg resection and its modifications are limb-sparing surgical options for tumors in this location.³ The relationship of the neurovascular bundle to the tumor and other structures of the shoulder girdle is the most significant anatomic factor in determining resectability and surgical reconstruction.

The resection and reconstruction of tumors of the shoulder girdle consists of three components: (1) surgical resection of the tumor following oncologic principles; (2) reconstruction of the skeletal defect (i.e., endoprosthetic replacement); and (3) soft-tissue reconstruction using multiple muscle transfers to cover the skeletal reconstruction and provide a functional extremity. The goal of all shoulder girdle reconstructions is to provide a stable shoulder and to preserve normal elbow and hand function. The extent of tumor resection and remaining motor groups available for reconstruction dictate the degree of shoulder motion and function.

PATIENT DEMOGRAPHICS AND CLINICAL OUTCOMES

The types of tumors, anatomic locations, and types of shoulder girdle resections performed in 143 patients treated at our institutions from 1980 to 1998 are shown in Figure 9.1B. Our experience with endoprosthetic reconstruction of the proximal humerus and scapula demonstrates that this is a reliable and durable technique of reconstruction. Survival rates based on Kaplan–Meier analysis demonstrate a 10-year survival

rate of 98–99% for proximal humeral replacements. There were no mechanical failures or dislocations. Other groups have reported a significant incidence of dislocation following endoprosthetic reconstruction of the shoulder girdle. This has not been our experience. Our results reflect the outcome of our use of "dual suspension" (i.e. static and dynamic) capsular reconstruction techniques and meticulous attention to soft-tissue reconstruction.

Historical Background

Some of the earliest discussions concerning limb-sparing surgery focused on techniques for resection of tumors about the scapula. Initial reports of shoulder girdle resections were confined to the individual bones or portions of the scapula. The first reported scapular resection was a partial scapulectomy performed by Liston in 1819⁴ for an ossified aneurysmal tumor. Between this time and the mid-1960s several other authors discussed limb-sparing resections about the shoulder girdle.^{5–11} In 1965 Papioannou and Francis¹² reported 26 scapulectomies and discussed the indications and limitations of the procedure.

The Tikhoff–Linberg interscapulothoracic resection, or triple-bone resection, was described by Baumann in 1914 in the Russian literature.¹³ He referred to a 1908 report by Pranishkov describing the removal of the scapula, the head of the humerus, the outer one-third of the clavicle, and the surrounding soft tissue for a sarcoma of the scapula. The shoulder was suspended from the remaining clavicle by metal sutures. Tikhoff and Baumann performed three such operations between 1908 and 1913, and Tikhoff was named as the originator of the procedure. The technique became established in the Western surgical community only after Linberg's 1926 English publication.³

Classically, most shoulder girdle resections were done for low-grade tumors of the scapula and for periscapular soft-tissue sarcomas. After the 1980s osteosarcoma and Ewing's sarcoma of the proximal humerus became the most common tumors treated with a Tikhoff–Linberg resection. A variety of new techniques and modifications of shoulder girdle resections have been developed. Most have been reported as "Tikhoff–Linberg" or modified "Tikhoff–Linberg" resections. These eponyms do not accurately describe the procedure performed, given that the Tikhoff–Linberg procedure was not intended to refer to sarcomas of the humerus.

Classification: Surgical Resection

Since 1965 several classification systems have been developed to describe shoulder girdle resections.¹⁴ The

earlier systems were purely descriptive and related almost exclusively to the bones resected. They did not accommodate or reflect concepts or terminology that have developed in the past two decades in orthopedic oncology.

The present surgical classification system was described by Malawer and associates in 1991 (Figure 9.2).¹⁵ It is based on the current concepts of surgical margins, the relationship of the tumor to anatomic compartments (intracompartmental vs. extracompartmental), the status of the glenohumeral joint, the magnitude of the individual surgical procedure, and precise considerations of the functionally important soft-tissue components. It has six categories, as follows:

- Type I : Intra-articular proximal humeral resection
- Type II: Partial scapular resection
- Type III: Intra-articular total scapulectomy

Type IV: Extra-articular total scapulectomy and humeral head resection (classical Tikhoff–Linberg resection)

Type V: Extra-articular humeral and glenoid resection

Type VI: Extra-articular humeral and total scapular resection

Each type is subdivided according to the status of the abductor mechanism (the deltoid muscle and rotator cuff):

A: Abductors intact

B: Abductors partially or completely resected

In general, Type A (abductors preserved) resections are intracompartmental and Type B (abductors resected) resections are extracompartmental.

This system is based on the anatomic and functional structures removed surgically. The six types are based

A

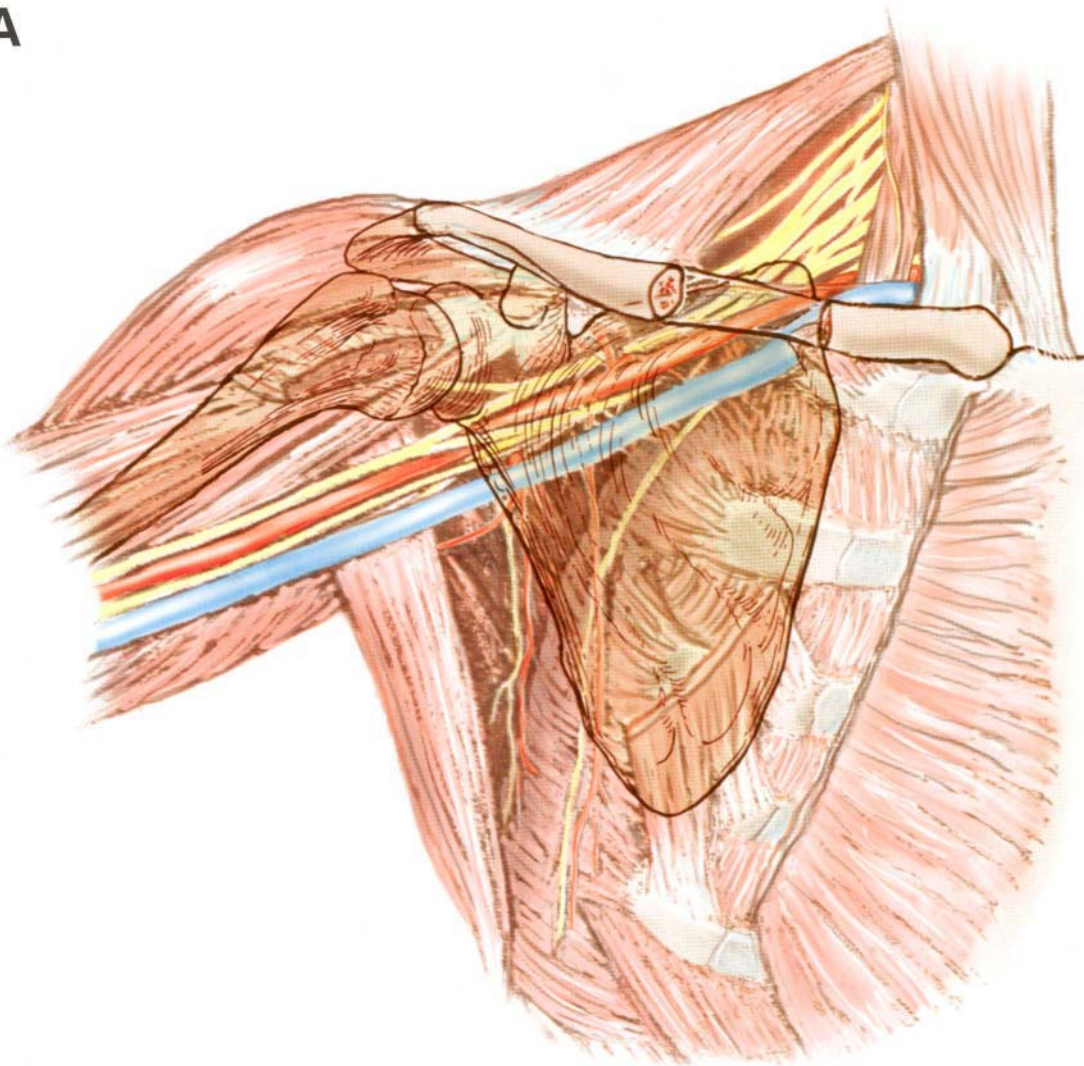


Figure 9.1 (see above and following page).

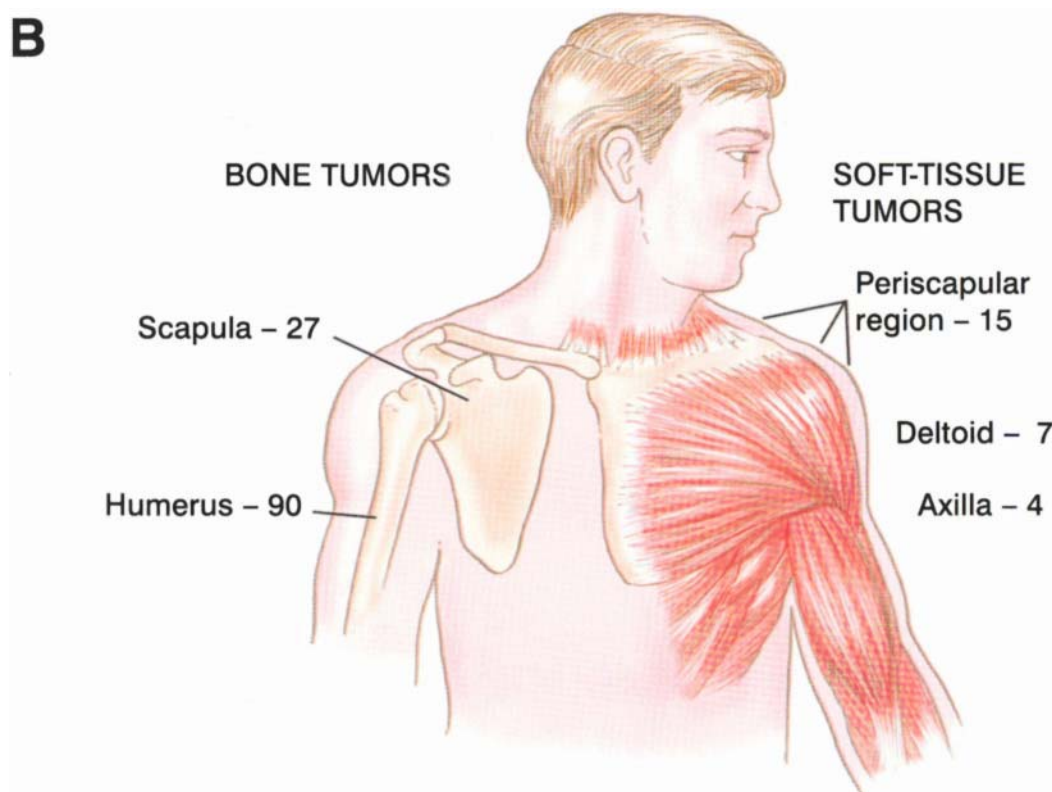


Figure 9.1 (A) Anatomy of shoulder girdle. (B) Schematic diagram of our combined* surgical experience in the treatment of shoulder girdle tumors (1980–1998). A total of 143 patients were treated by limb-sparing procedures. There were 117 bone and 15 periscapular soft-tissue tumors. *Combined experience of Martin M. Malawer, M.D., Washington, DC, and Isaac Meller, M.D., Tel-Aviv, Israel.

Table 9.1 Histologic classification and anatomic location of bone and soft-tissue tumors around the shoulder girdle of 143 patients treated between 1980 and 1998

Tumor histologic type	Anatomic location (no. of patients)				
	Proximal humerus	Scapula	Proximal arm	Periscapula	Axilla
Primary bone sarcomas					
Osteosarcoma	40	6			
Chondrosarcoma	29	5	–	–	–
Ewing's sarcoma	3	5	–	–	–
Other primary malignancies of bone	2	5	–	–	–
Metastatic bone disease	11	1	–	–	–
Benign-aggressive bone tumors	5	5	–	–	–
Soft-tissue sarcoma	–	–	6	13	4
Benign-aggressive soft-tissue tumors	–	–	1	2	–
<i>Totals</i>	90	27	7	15	4

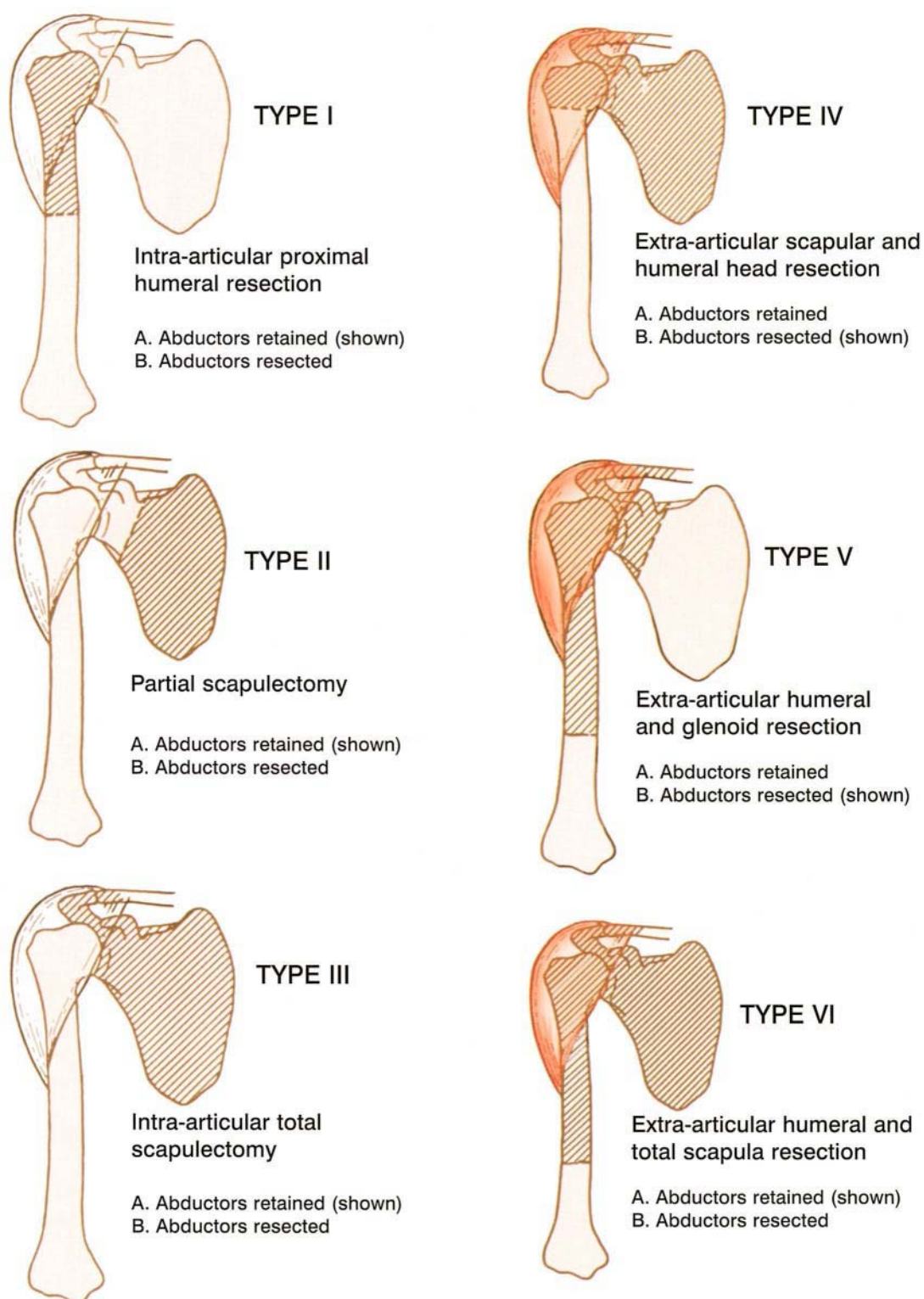


Figure 9.2 Surgical classification of shoulder girdle resections. This system was initially proposed by the senior author in 1991. Types I–III are intra-articular resections, whereas Types IV–VI are extra-articular resections. A = abductor muscles retained, B = abductor muscles resected (see text). (Clin Orthop 1991 Jun (267): 33–44)

on the bony segments involved and their relationship to the glenohumeral joint. The distinguishing variable is the status of the main motor group, the abductor mechanism. The loss of any component of the abductor mechanism (deltoid or rotator cuff muscles) creates a similar functional disability. The abductor mechanism is almost always resected when there is extraosseous extension of a bone tumor in this area.

Type I–VI shoulder girdle resections and their indications are briefly described below. The surgical technique for each resection and reconstruction are described in Chapters 33 and 34.

Type I Resection (Figure 9.3)

The least frequently performed shoulder girdle resection, this procedure is an intra-articular resection of the proximal humerus. It is performed for some low-grade tumors and, rarely, for high-grade tumors of the proximal humerus that have no extraosseous component (Stage IIA). Metastatic disease of the proximal humerus with extensive destruction of bone or a pathologic fracture can also be treated with a Type I resection. Reconstruction is performed using an endoprosthesis and local muscle transfers. A Gore-Tex graft reconstruction of the glenohumeral joint capsule may be required following a Type I resection, even when normal soft tissues are retained to provide stability (see Chapter 33).

Type II Resection (Figure 9.4)

This procedure is a partial scapulectomy of the scapular body. It is usually performed for low-grade osseous malignancies of the scapula that involve the medial scapular body. It is rarely indicated for small high-grade malignancies in this location. Soft-tissue sarcomas that secondarily invade the medial scapula may also be treated by this resection. Occasionally, a limited chest wall resection beneath the partial scapulectomy is required to achieve a negative margin of excision. Reconstruction is performed using local muscle transfers and attaching these to the remaining scapula.

Type III Resection (Figure 9.5)

This resection is an intra-articular total scapulectomy. It is most frequently performed for soft-tissue sarcomas that secondarily invade the scapula and for primary osseous malignancies of the scapular body that do not invade the glenohumeral joint. Reconstruction is performed using a total scapular prosthesis if adequate soft tissues remain for reattachment to stabilize the

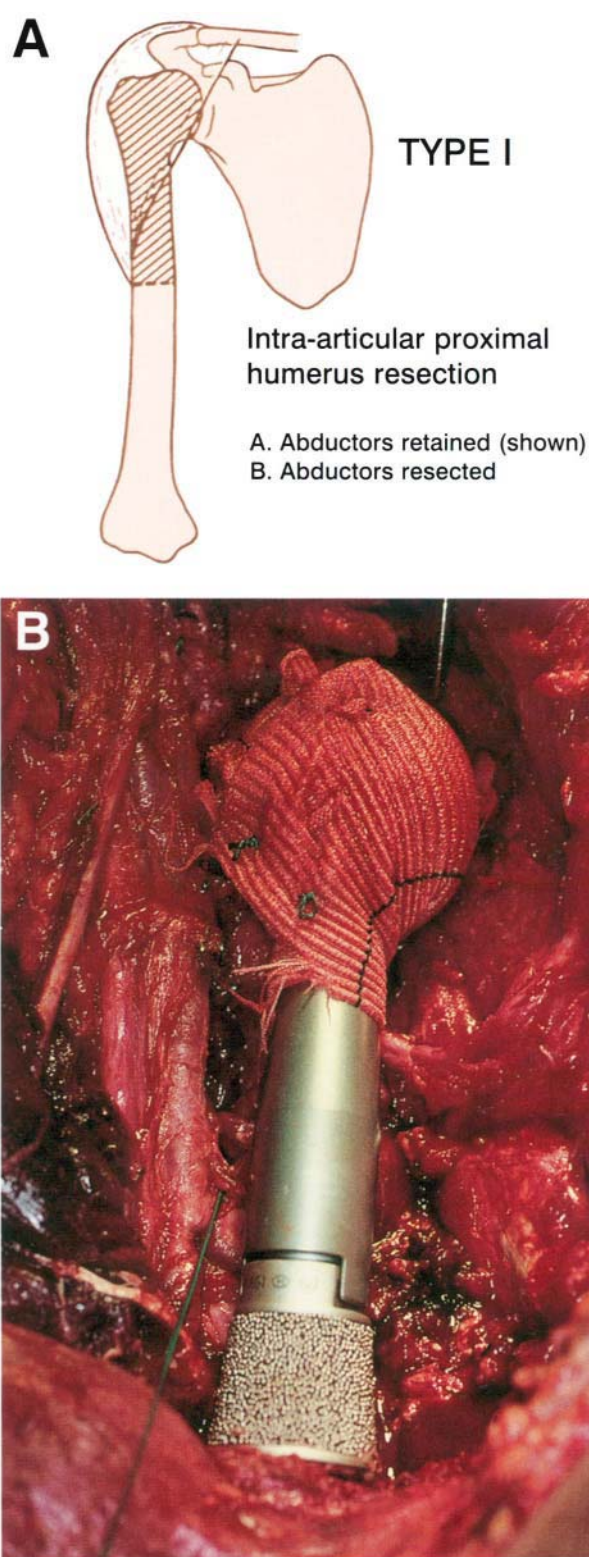


Figure 9.3 (A) Type I shoulder girdle resection; (B) intraoperative photograph of a Type I proximal humeral resection and reconstruction. This patient was reconstructed with a proximal humeral prosthesis (MRS) and a Gore-Tex graft to reinforce the capsule.

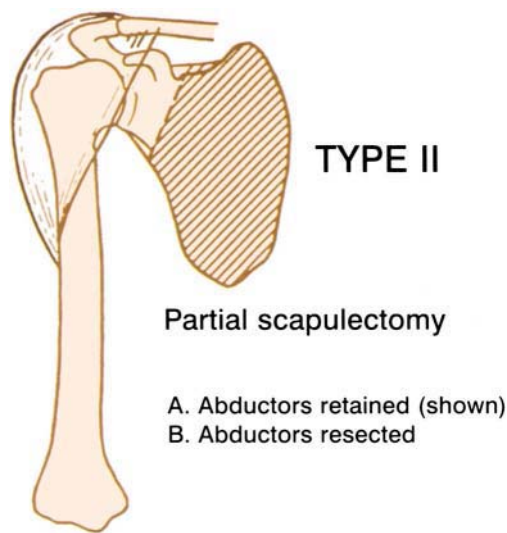


Figure 9.4 Type II shoulder girdle resection.

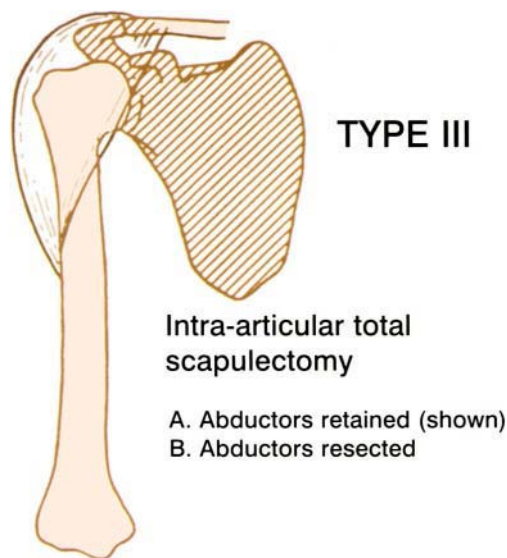


Figure 9.5 Type III shoulder girdle resection.

prosthesis. Otherwise, the proximal humerus is suspended from the distal clavicle and adjacent muscles are transferred to provide stability.

Type IV Resection: The Tikhoff–Linberg Procedure (Figure 9.6)

This procedure is an extra-articular en-bloc resection of the scapula, glenohumeral joint and humeral head, and distal clavicle. It is indicated for high-grade malignancies of the scapula, especially if the tumor extends

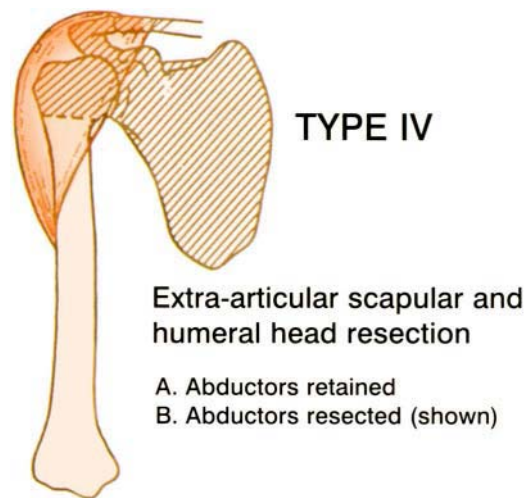


Figure 9.6 Type IV shoulder girdle resection. This is the original Tikhoff–Linberg resection of the shoulder girdle.

anteriorly or laterally and involves the rotator cuff, or there is invasion of the glenohumeral joint. This procedure is also used for some low-grade sarcomas of the scapula and for periscapular soft-tissue sarcomas. Most malignant tumors of the scapular neck or glenoid require this approach.

The extent of proximal humeral resection and the remaining muscle available for reconstruction and coverage dictate the type of reconstruction that is performed. If adequate soft tissue is preserved, a total scapula and shoulder joint prosthesis is used (Figure 9.7). Otherwise, local muscle reconstruction and a dual-suspension technique using Dacron tape to suspend the proximal humerus from the remaining clavicle is performed (see Chapter 33).

Type V Resection (Figure 9.8)

This resection is the most common procedure for high-grade sarcomas of the proximal humerus. It involves an extra-articular, en-bloc resection of the proximal humerus, distal clavicle, and glenohumeral joint. The scapular resection is performed through the scapular neck, just medial to the coracoid. The axillary nerve and shoulder abductors are routinely sacrificed because of the extraosseous extension of tumors in this location (Figures 9.9 and 9.10).

Reconstruction of the osseous defect is performed using the modular proximal humerus endoprosthesis in conjunction with the dual-suspension technique described in Chapters 33 and 34 (Figure 9.11). This is combined with multiple muscle transfers to reconstruct all soft tissues that have been resected.

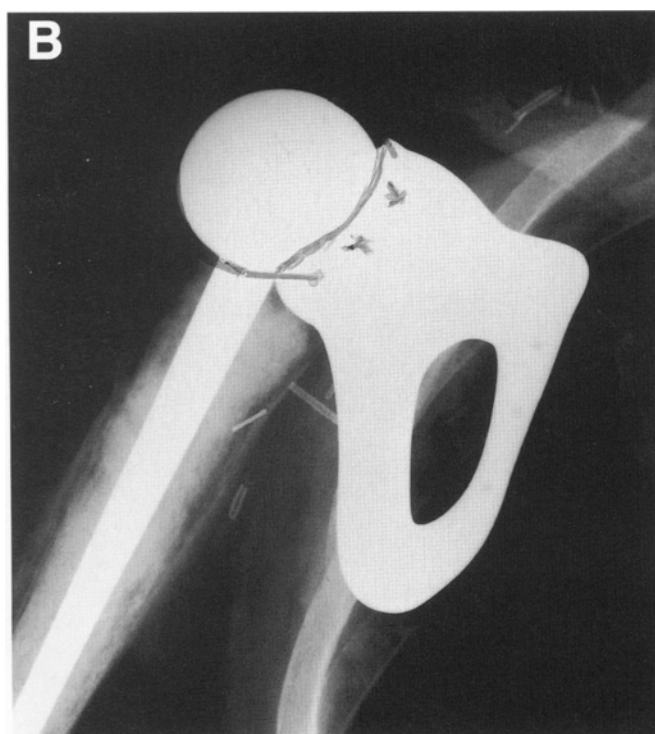
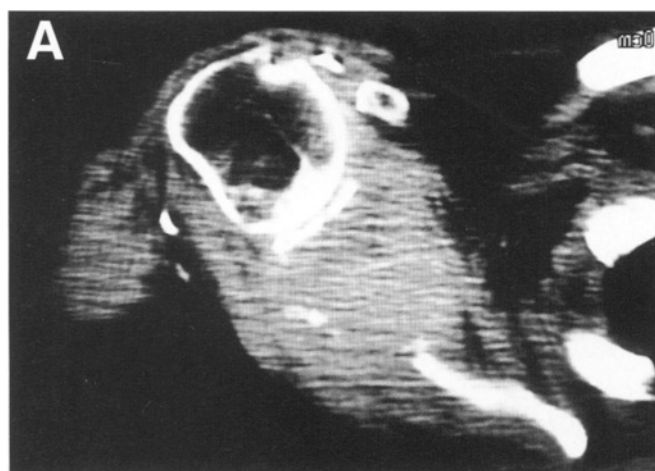


Figure 9.7 (A) Large Ewing's sarcoma of the scapula that involves the glenohumeral joint with a large extraosseous soft-tissue component. This patient was treated with induction chemotherapy followed by an extraarticular resection of the scapula and the humeral head (Type IV resection). This was reconstructed by a scapular prosthesis. A Gore-Tex graft was used to reconstruct the capsule and to restore stability. (B) Plain radiograph following reconstruction. The Gore-Tex is outlined in black and the Dacron sutures that attach the Gore-Tex graft to holes in the scapular prosthesis are marked by the small x.

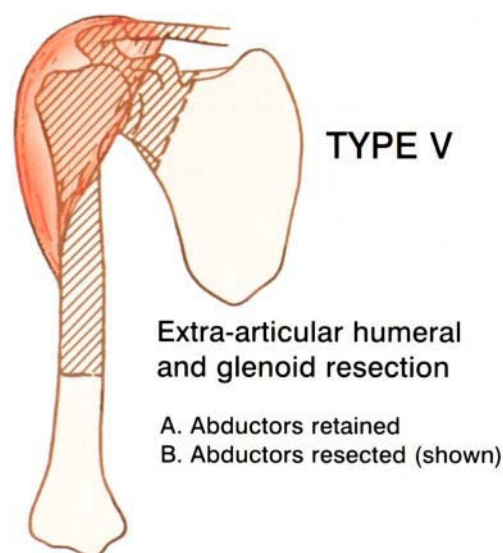


Figure 9.8 This is the type of resection recommended by the authors for most stage IIB proximal humeral osteosarcomas.

Type VI Resection (Figure 9.12)

This procedure is performed less frequently than Type V resections and is usually used for large advanced sarcomas of the proximal humerus that cross the shoulder joint and invade the scapula. High-grade soft-tissue tumors located over the glenohumeral joint, with or without osseous extension, may require this type of resection. The procedure involves resection of the proximal humerus and distal clavicle, and an extra-articular en-bloc resection of the glenohumeral joint and entire scapula.

UTILITARIAN SHOULDER GIRDLE INCISION (Figure 9.13)

The utilitarian shoulder girdle incision consists of an anterior and posterior component. This incision, or parts of it, permits adequate exploration and resection of the humerus, scapula, or axilla. It provides for safe exposure of the axillary vessels and brachial plexus.

Anteriorly, the incision begins at the junction of the inner and middle thirds of the clavicle, continues over the coracoid process and along the deltopectoral groove, and down the arm over the medial border of the biceps muscle. The posterior incision begins over the mid-clavicular portion of the anterior incision (crossing the suprascapular area) and runs over the lateral aspect of the scapula, and then curves posteriorly. Large fasciocutaneous (axilla) flaps are elevated anteriorly and posteriorly.

Resection of a tumor in the proximal humerus, proximal arm, or axilla utilizes the anterior component.

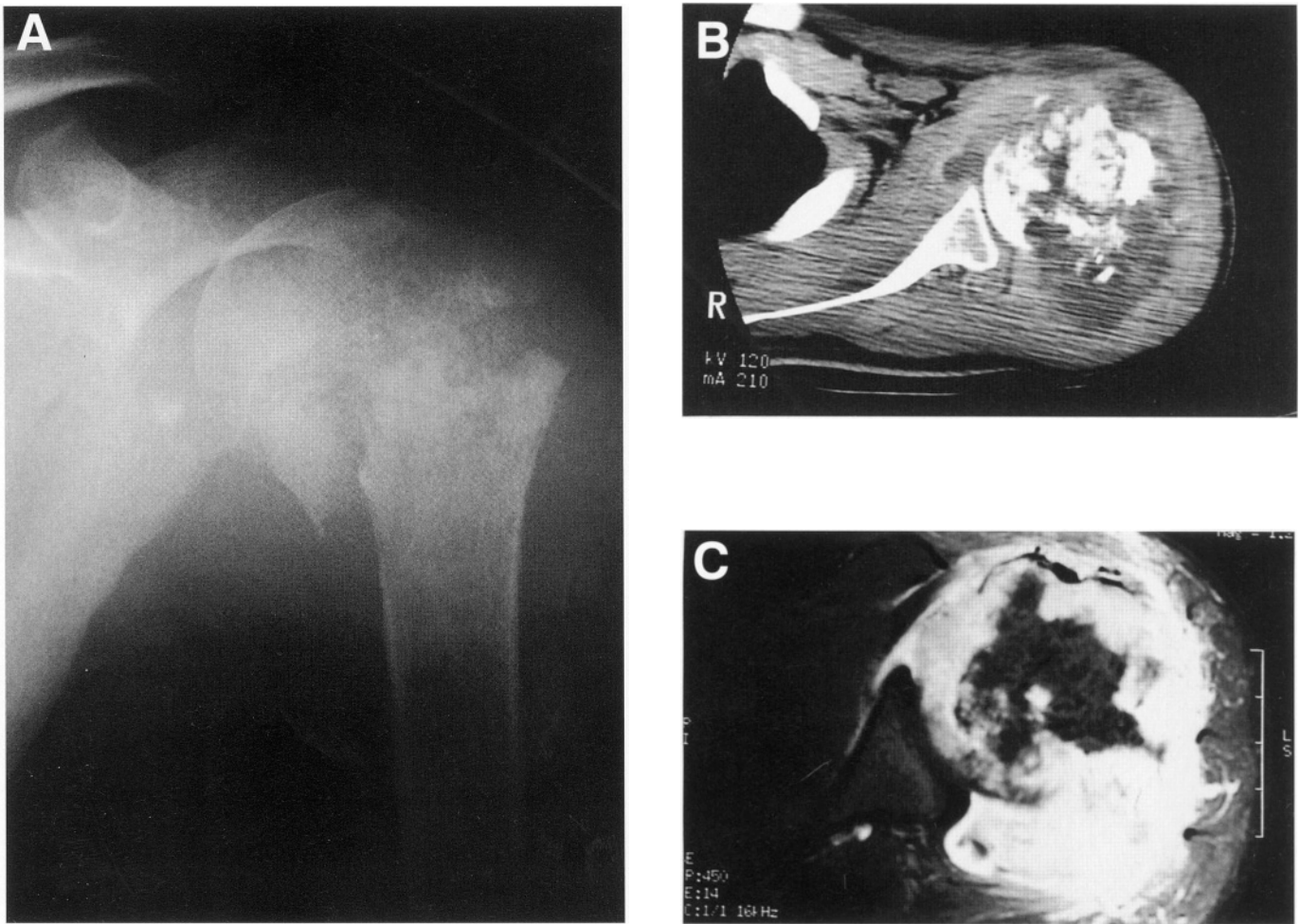


Figure 9.9 (A) Plain radiograph of an osteosarcoma of the proximal humerus with a pathologic fracture. In general, osteolytic osteosarcoma is the specific type of osteosarcoma that may develop a pathologic fracture. (B) CT scan showing a large soft-tissue component at the fracture site. Note the extension around the glenohumeral joint. Tumors of the proximal humerus may often involve the glenoid and are therefore treated by extra-articular resection (Type V). (C) MRI of the same patient showing extensive tumor involvement of the glenohumeral joint and pericapsular mechanisms.

It starts with the exposure of the main neurovascular bundle of the upper extremity. It is performed by a deltopectoral incision, detachment, medial reflection of the humeral insertion of the pectoralis major muscle, and with detachment and reflection of the coracoid origins of the pectoralis major, coracobrachialis, and short head of the biceps muscle. The posterior component of the utilitarian incision is used for resections around the scapula and glenoid: if the resection is performed close to the neurovascular bundle as in the case of an extra-articular resection of the scapula, the anterior incision is required to expose the neurovascular structure. The posterior incision permits wide exposure of the scapula, rhomboids, latissimus dorsi, and trapezius muscles.

We have found this incision permits safe exposure for resection and reconstruction of most shoulder girdle tumors.

INDICATIONS AND CONTRAINDICATIONS TO LIMB-SPARING SURGERY

Indications for limb-sparing procedures include high-grade and some low-grade bone and soft-tissue sarcomas of the shoulder girdle. Occasionally, benign-aggressive tumors may also require these treatment techniques. Selection of patients for this procedure is based on the anatomic location of the tumor and a thorough understanding of the natural history of sarcomas and other malignancies.

Absolute contraindications for limb-sparing procedures include tumor involvement of the neurovascular bundle, or a patient's inability or unwillingness to tolerate a limb-sparing operation. Relative contraindications may include chest wall extension, pathologic fracture, previous infection, lymph node involvement

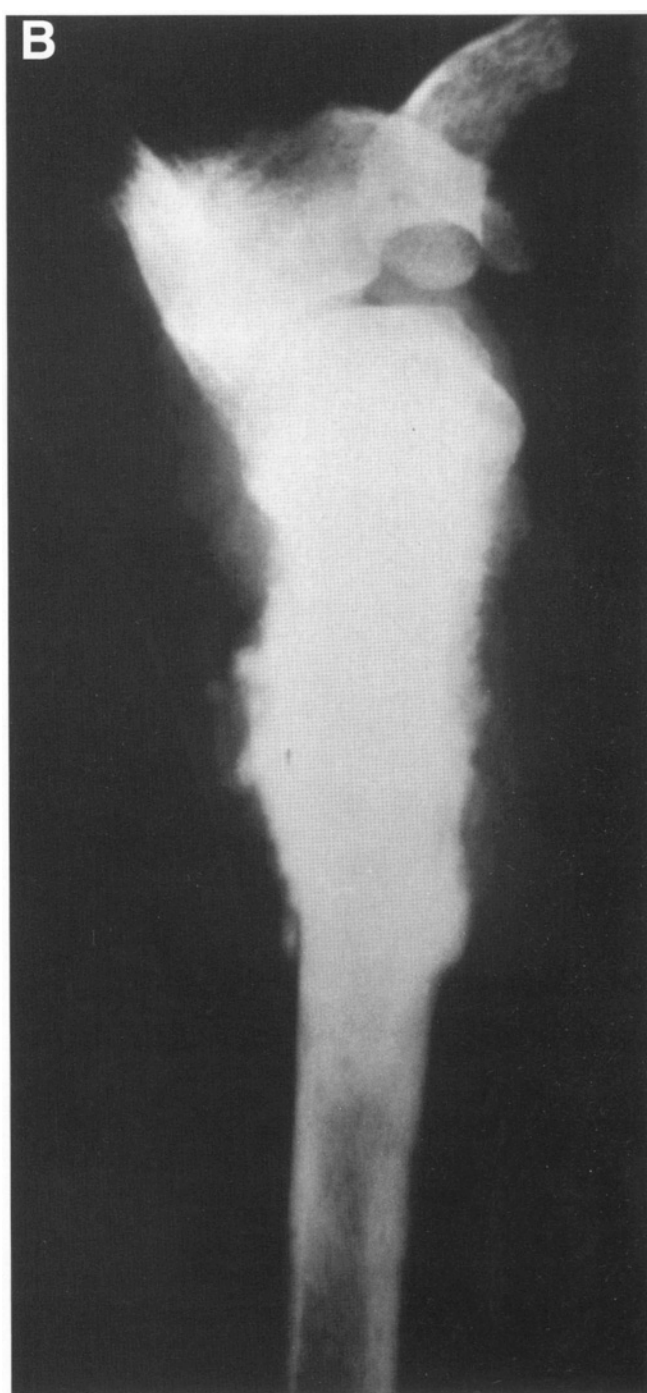
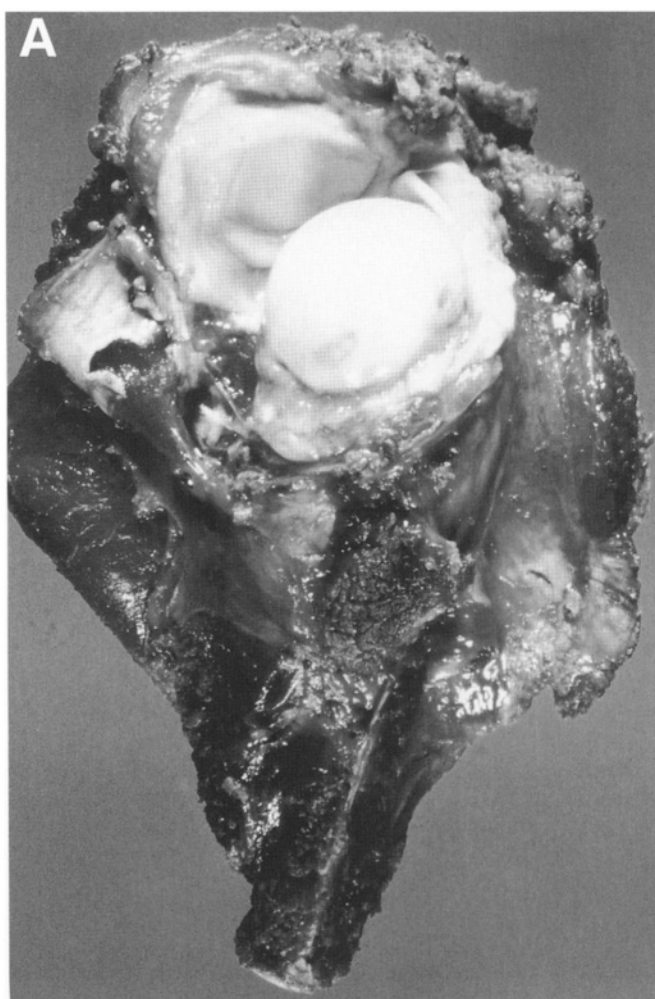


Figure 9.10 (A) Gross specimen following an extra-articular resection of the proximal humerus. Extra-articular resections are routinely performed for high-grade sarcomas of the proximal humerus. The glenohumeral joint is removed en-bloc with the adjacent deltoid muscle, axillary nerve, and rotator cuff musculature. The local recurrence rate following extra-articular resection is less than 2%. (B) Plain radiograph of a gross specimen following an extra-articular resection of the proximal humerus. This illustrates a sclerosing osteosarcoma that has been removed en-bloc with the glenoid and a portion of the clavicle. (Clin Orthop 1991 Jun (207): 33–44)

or a complicated, inappropriately placed biopsy that has resulted in extensive hematoma and tissue contamination.

Biopsy Site

One of the most common causes for forequarter amputation is an inappropriately placed biopsy that has resulted in contamination of the pectoralis muscles, neurovascular structures, and chest wall. Extreme care

must be taken with the biopsy placement and technique (see Biopsy Technique section).

Vascular Involvement

Fortunately, most tumors of the proximal humerus are separated from the anterior vessels by the subscapularis muscle and short head of the biceps. It is rare for the axillary or brachial artery to be involved with tumor, although a large soft-tissue component may cause

displacement and compression. In general, if the vessels appear to be involved with tumor, the adjacent brachial plexus is also involved, and a limb-sparing procedure may be contraindicated.

Nerve Involvement

The three major cords of the brachial plexus follow the artery and vein and are rarely involved with tumor.

Two of its major branches, the axillary and musculocutaneous nerves, may be involved. Resection of the axillary nerve is usually required for Stage IIB tumors of the proximal humerus. The radial nerve is rarely involved. The deficit created by resecting the radial nerve is greater than that for the musculocutaneous nerve, but this should not be an indication for amputation. If the resection will lead to a major functional loss and a close margin (increasing the risk of

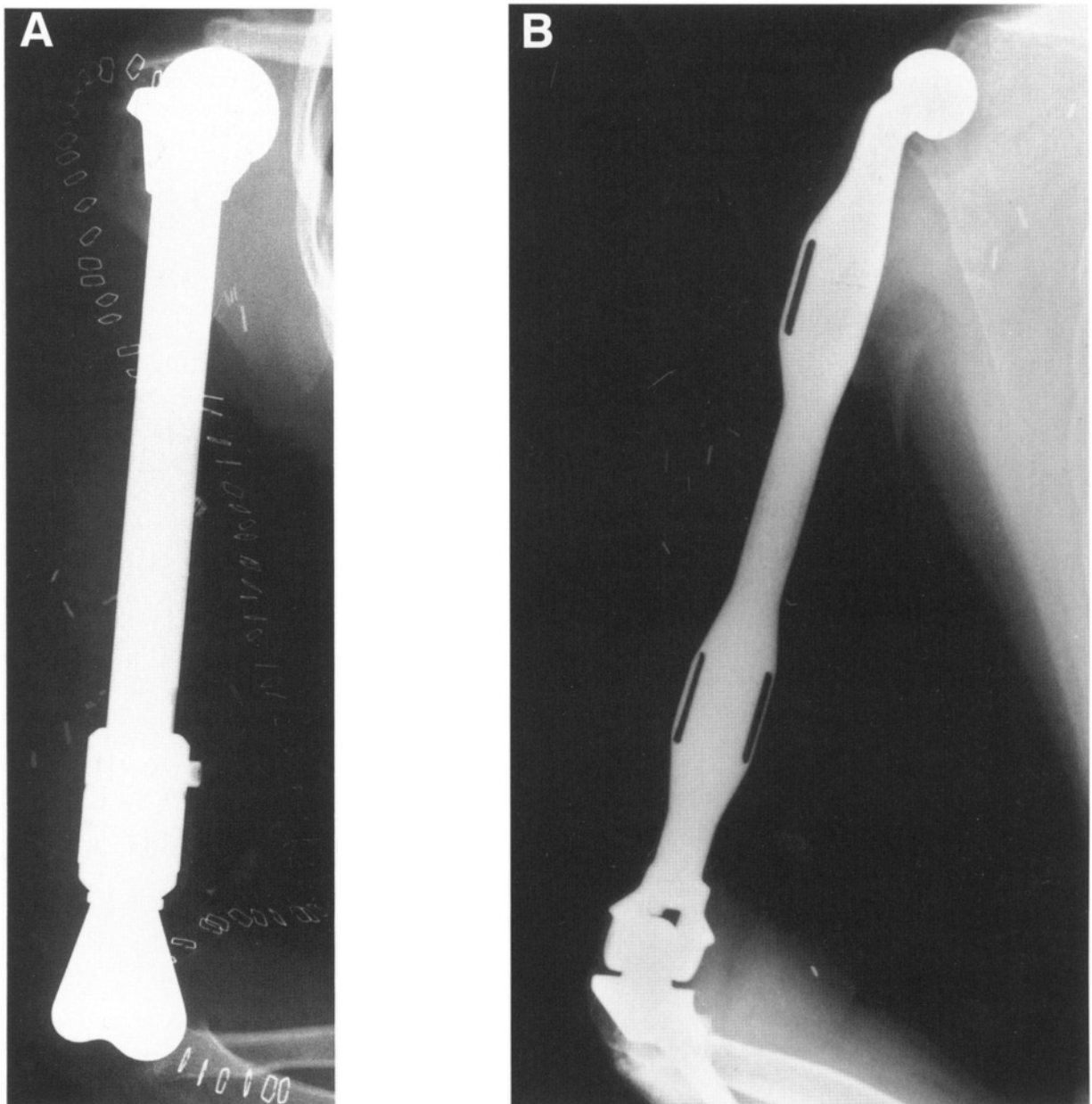


Figure 9.11 Total humeral prosthesis following an extended Type V resection. (A) An expandable total prosthesis utilized in a 6-year-old child for a diaphyseal osteosarcoma. (B) A solitary total humerus with an elbow joint utilized in a skeletally mature adolescent.

local recurrence), amputation should be considered. Direct tumor extension into the brachial plexus necessitates a forequarter amputation.

Lymph Nodes

Bone sarcomas rarely involve adjacent lymph nodes; nevertheless, axillary nodes should be evaluated and may require biopsy. In the rare incidence of lymph node involvement documented by biopsy, a forequarter amputation may be the best method for removing all gross disease. Alternatively, a lymph node dissection in conjunction with a limb-sparing procedure may be considered. It is the author's experience (Malawer), based on two cases, that local control and long-term survival can be obtained by this method.

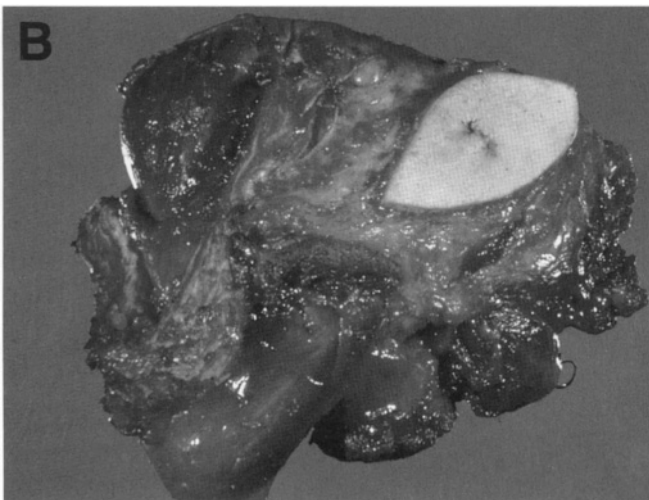
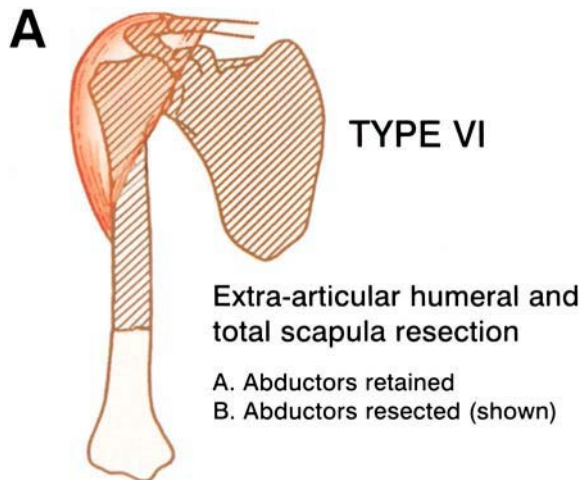


Figure 9.12 (A) Type VI shoulder girdle resection. (B) Gross specimen of a total scapula and total humerus resection.

Chest Wall Involvement

Tumors of the shoulder girdle with large extrasosseous components may occasionally involve the chest wall, ribs, and intercostal muscles. This should be evaluated preoperatively with physical examination and imaging studies; however, such involvement is often not determined until the time of surgery. This is not an absolute indication for forequarter amputation; a limb-sparing procedure combined with a chest wall resection may be performed, depending on the involvement of adjacent soft tissues and neurovascular structures.

Previous Resection

The local recurrence rate is increased if a wide resection is attempted following a previous resection around the shoulder girdle. This is especially true of tumors of the scapula and clavicle and for tumors of the proximal humerus that involve the surrounding soft tissues.

Infection

In patients with high-grade sarcomas, limb-sparing procedures performed in an area of infection are extremely risky, because these patients must receive postoperative adjuvant chemotherapy. If an infection cannot be eradicated with the primary resection, amputation is advisable.

Preoperative Evaluation and Imaging

Physical examination, plain radiographs, computerized tomography and magnetic resonance imaging, arteriography and bone scan (total-body and three-phase) are important means of evaluating a patient with a tumor of the shoulder girdle. For large tumors of the proximal humerus a venogram may also be a useful study if there is evidence of distal obstruction suggesting intravascular tumor thrombus (analogous to tumor thrombi seen in the iliac vessels from large pelvic sarcomas).

Physical Examination

The physical examination is important in determining tumor extension into the glenohumeral joint, neurovascular involvement, or tumor invasion of the chest wall. If tumor has invaded the joint, shoulder range of motion is generally reduced and the patient may complain about discomfort and pain. Neurovascular involvement or compression may be suggested by an abnormal neurovascular exam or by decreased or absent pulses. Tumors that move freely with respect to the chest wall are usually separated from it by at least a thin tissue plane through which it is safe to dissect.

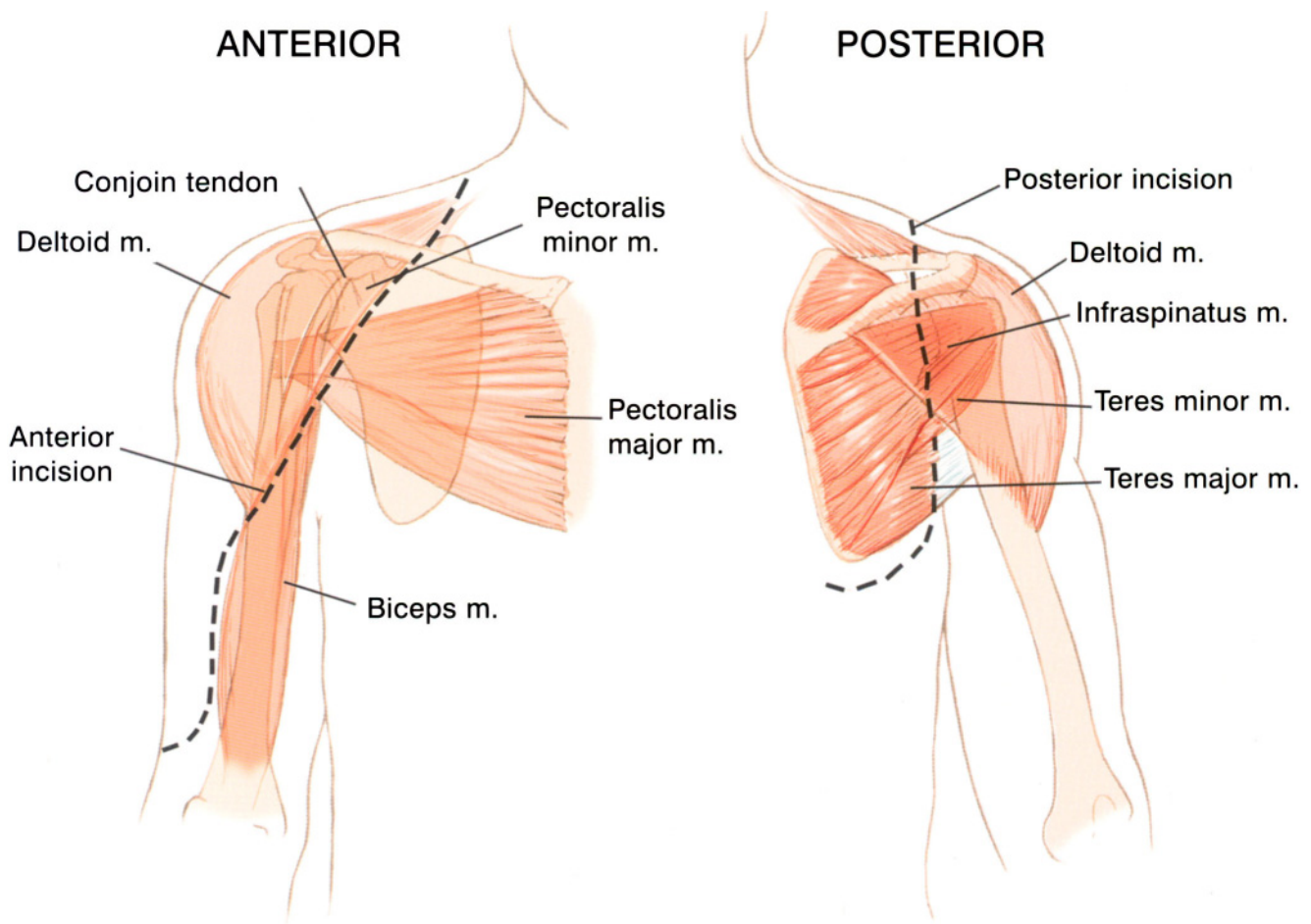


Figure 9.13 Utilitarian shoulder incision used by the authors for exposure of the proximal humerus, scapula, and/or shoulder girdle.

Imaging Studies

These are extremely important in determining the exact anatomic location and extent of tumor involvement (Figure 9.14). The specific information gained from each modality is as follows:

Bone scan

This study helps determine intraosseous tumor extent and detects metastases. It may also indicate rib involvement or extension of the tumor across the joint with further invasion of the adjacent bone. The blood flow portion (three-phase study) helps determine tumor vascularity.

MRI

This scan is useful to determine the extent of soft-tissue involvement and tumor extension into the joint or

chest wall. It is especially useful in evaluating tumors of the suprascapular region that may extend below the subscapularis muscle and exit near the coracoid. The location of vessels, which directly correlates to the position of the nerves, can also be visualized. The intraosseous tumor extent can also be evaluated, and this is necessary for determining the location of required bone resection. All three planes should be examined. MRI has not been reliable in determining tumor response to induction chemotherapy (Figure 9.15).

CT

CT is considered complementary to MRI in evaluating the chest wall, clavicle, and axilla. Compared with MRI it is more useful in determining cortical bone changes or destruction, and is more reliable in determining the bone response and effects of induction chemotherapy (Figure 9.9B).

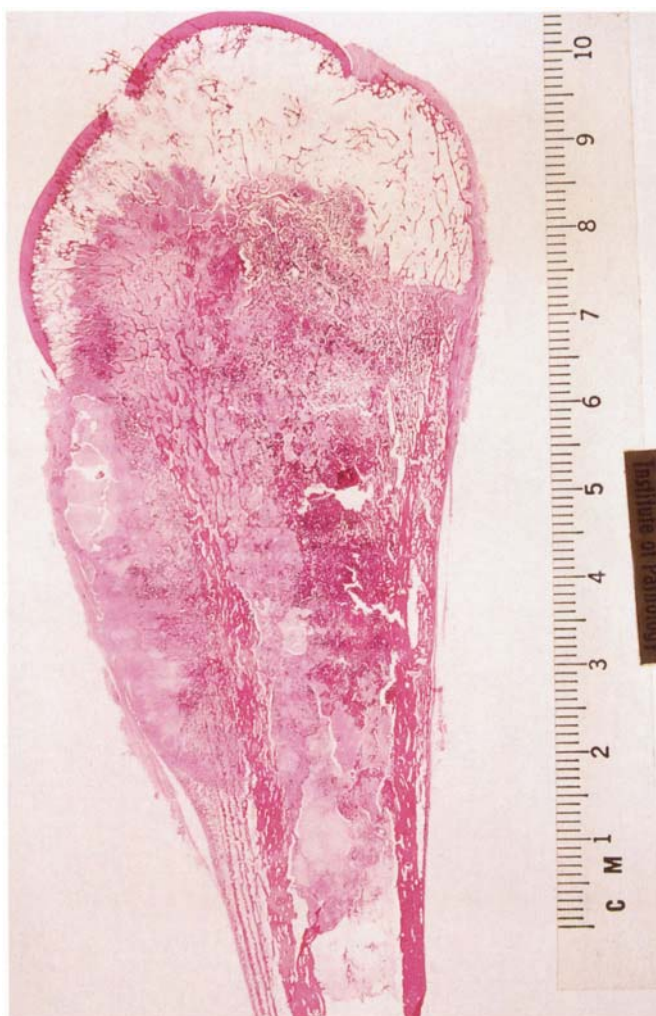


Figure 9.14 Macrospecimen following resection of osteosarcoma of the proximal humerus. Note that the tumor is filling up the intramedullary canal as well as a small soft-tissue component projecting laterally. Ninety-five percent of osteosarcomas have extraosseous components.

Angiography

Although vessels can be visualized using MRI, arteriography remains the most useful study for determining the relationship of the tumor to the brachial plexus and vessels, as well as depicting the exact level of the circumflex vessels and any anatomic variants or anomalies. This is also the most useful study in predicting the tumor response to induction chemotherapy. Tumor necrosis is directly related to the decrease or absence of tumor vascularity.

DETERMINING RESECTABILITY OF SHOULDER GIRDLE TUMORS (Figures 9.15B and C)

High-grade tumors arising from the shoulder girdle region are frequently large and encroach upon the neurovascular bundle. Tumors that encase or invade the brachial plexus are considered unresectable. It is difficult to clinically determine which tumors are unresectable. Based on our experience we have found the clinical triad of intractable pain, motor deficit, and venogram showing obliteration of the axillary vein to be very reliable in predicting brachial plexus invasion. There is no single imaging study that accurately visualizes the brachial plexus. MRI and CT scans typically show a large tumor juxtaposed to the neurovascular bundle. Venography, however, is extremely accurate in predicting brachial plexus invasion. The axillary vein, axillary artery and brachial plexus travel in intimate association within a single fascial sheath (axillary sheath). The major nerves and cords form the periphery of the sheath; therefore only obliteration (not just compression) of the brachial or axillary vein denotes direct tumor extension in and around the nerves. This indicates secondary involvement of the venous wall. This progression also explains the clinical triad of pain, motor loss, and venous obstruction. Tumors that invade or encase the brachial plexus obliterate the axillary vein because of its thin walls and low intraluminal pressure. In these instances arteriography demonstrates displacement of the axillary artery; however, the axillary artery remains patent because of its thick walls and high intraluminal pressures. The final decision, however, regarding the need for a forequarter amputation should be reserved until surgical exploration of the brachial plexus has been performed (Figure 9.15).

Biopsy Technique

The biopsy site should be carefully selected. It should be located away from the major vessels and nerves and placed so that it can be widely excised by the definitive resection. Inadvertent contamination of the neurovascular structures or the chest wall must be avoided. Sarcomas of the shoulder girdle rarely require an open biopsy. The majority of sarcomas in this location have an extraosseous (soft-tissue) component; therefore, a small-needle or core biopsy should be performed (Figure 9.16).

All fine-needle or core biopsies should be performed under fluoroscopic or CT guidance unless a mass is easily palpable and located away from the neurovascular bundle. Only one puncture site is required. The needle is then reintroduced through the same puncture site, but the angle is varied so that cores can be obtained from several different regions of the tumor. Touch-

preps and frozen sections are performed at the time of biopsy to confirm that adequate intralesional tissue has been obtained for diagnosis. Cultures are routinely obtained, irrespective of the suspected diagnosis, because an infection may simulate any malignancy.

Proximal Humerus

Needle or incisional biopsies of tumors of the proximal humerus should be performed through the anterior one-third of the deltoid muscle, not through the deltopectoral interval. A biopsy through the anterior one-third of the deltoid results in a limited hematoma, that is confined by the deltoid muscle. This portion of the muscle and biopsy hematoma are easily removed at the definitive resection. A biopsy through the deltopectoral interval will contaminate the pectoralis muscle which is necessary for reconstruction and increase the risk that a hematoma may spread along the brachial

vessels to the chest wall, making a local resection difficult, if not impossible.

If an open biopsy is required, a short longitudinal incision should be made just lateral to the deltopectoral interval. The dissection should be directly into the deltoid muscle and proximal humerus. The bone should be exposed lateral to the long head of the biceps. No flaps should be developed, and the glenohumeral joint should not be entered.

Scapula

Biopsies of the scapular body are more difficult to perform than biopsies of the proximal humerus; however, they are crucial in determining the final operative procedure. The biopsy site should be along the intended incision site of the resection. A posterior needle biopsy is recommended for tumors arising within the body of the scapula; the anterior approach should be avoided.

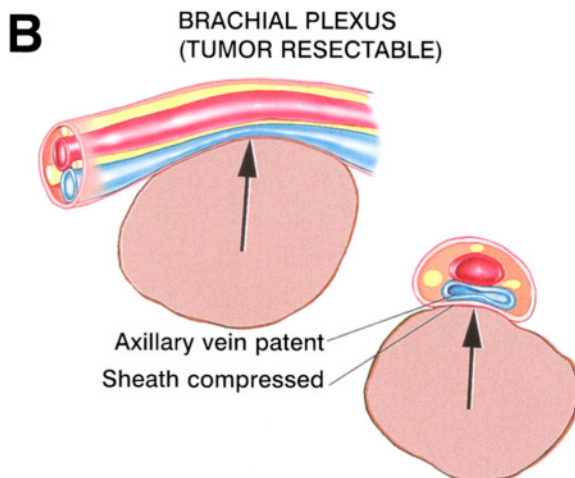
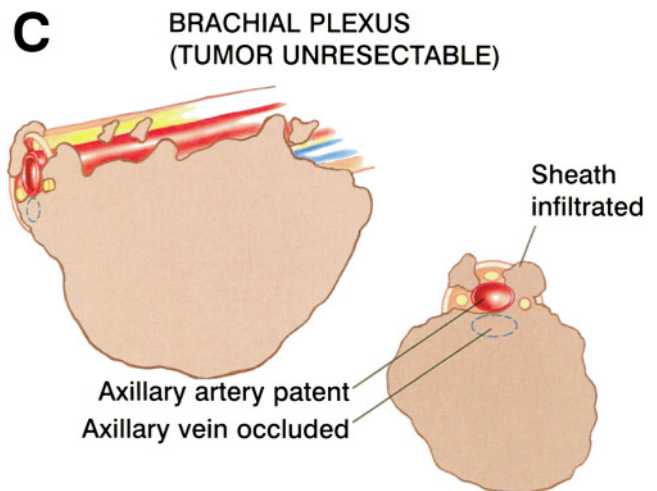
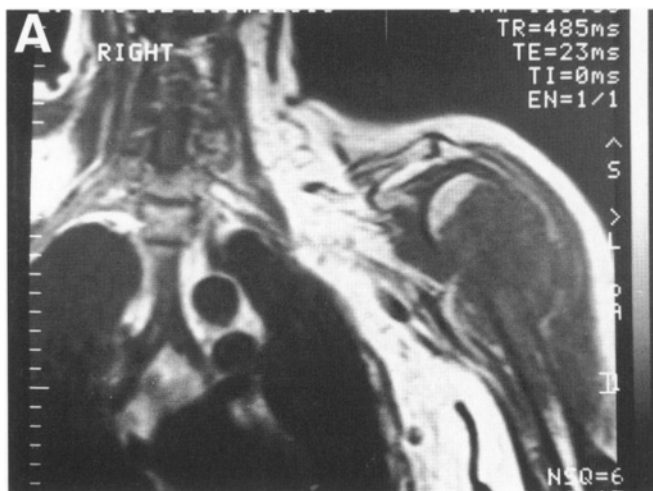


Figure 9.15 (A) MRI of a typical osteosarcoma of the proximal humerus. Note the involvement of one-third of the proximal humerus with a large extraosseous component below the deltoid muscle. CT and MRI are used concurrently to determine the bony and soft-tissue details when evaluating sarcomas. The deltoid muscle and the axillary nerve are often resected when performing a limb-sparing procedure. (B) Schematic demonstrating a resectable tumor. The tumor is compressing and displacing the neurovascular bundle; however, there is no invasion or encasement. This situation most commonly arises in the treatment of a sarcoma. An arteriogram and venogram would show patency of the axillary artery and vein. (C) Schematic demonstrating an unresectable tumor. The tumor is infiltrating the neurovascular structures and obliterating the axillary vein. Venography would show an obliterated axillary vein. Arteriography would show a displaced but patent axillary artery.

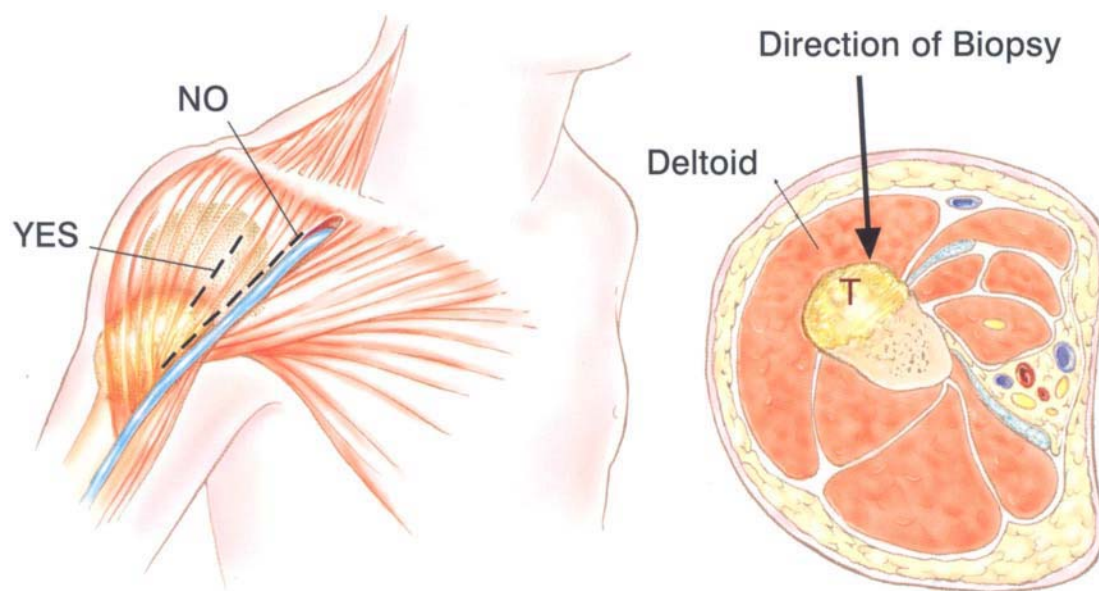


Figure 9.16 Schematic diagram of biopsy technique for tumors of the proximal humerus. The biopsy should be performed through the anterior one-third of the deltoid. The deltopectoral groove must be avoided. A core biopsy is recommended. An open biopsy should be performed only if a core needle biopsy is nondiagnostic. (Clin Orthop 1999 Nov (368): 210–219)

Biopsies of tumors in the lateral aspect of the scapula or glenoid region should be performed along the lateral or axillary aspect of the scapula, directly through the posterior deltoid and teres minor.

Clavicle

Unless a soft-tissue component is present, a small open biopsy of the clavicle is advisable. A needle may injure the underlying neurovascular structures. Biopsies of the clavicle are done through an incision that is parallel to the long axis of the clavicle. Care should be taken not to dissect circumferentially around the clavicle. As with all incisional biopsies, hemostasis needs to be obtained before closing the biopsy incision.

SURGICAL AND ANATOMIC CONSIDERATIONS

A limb-sparing procedure involving the shoulder girdle is more difficult than a forequarter amputation. The surgical options are technically demanding and are fraught with potential complications. The local anatomy of the tumor often determines the extent of the required resection. One should be experienced with all aspects of shoulder girdle anatomy and familiar with several unique anatomic considerations.

"FUNCTIONAL COMPARTMENT" OF THE SHOULDER (Figure 9.17A–C)

Sarcomas grow locally in a centripetal manner and compress surrounding tissues (muscles) into a pseudocapsular layer. The pseudocapsular layer contains microscopic finger-like projections of tumor referred to as satellite nodules. Sarcomas spread locally along the path of least resistance. Surrounding fascial layers resist tumor penetration and therefore provide boundaries to local sarcoma growth. These boundaries form a compartment around the tumor. A sarcoma will grow to fill the compartment in which it arises, and only rarely will an extremely large sarcoma extend beyond its compartmental borders. In discussing bony sarcomas that extend beyond the cortices into the surrounding soft tissues, a functional anatomic compartment refers to the investing muscles that are compressed into a pseudocapsular layer. These muscles provide the fascial borders of the compartment that has important surgical implications. A wide resection of a bone sarcoma removes the entire tumor and pseudocapsular layer and must therefore encompass the investing muscle layers (compartmental resection).

The functional compartment surrounding the proximal humerus consists of the deltoid, subscapularis and remaining rotator cuff, latissimus dorsi (more distally), brachialis, and portions of the triceps muscles. The

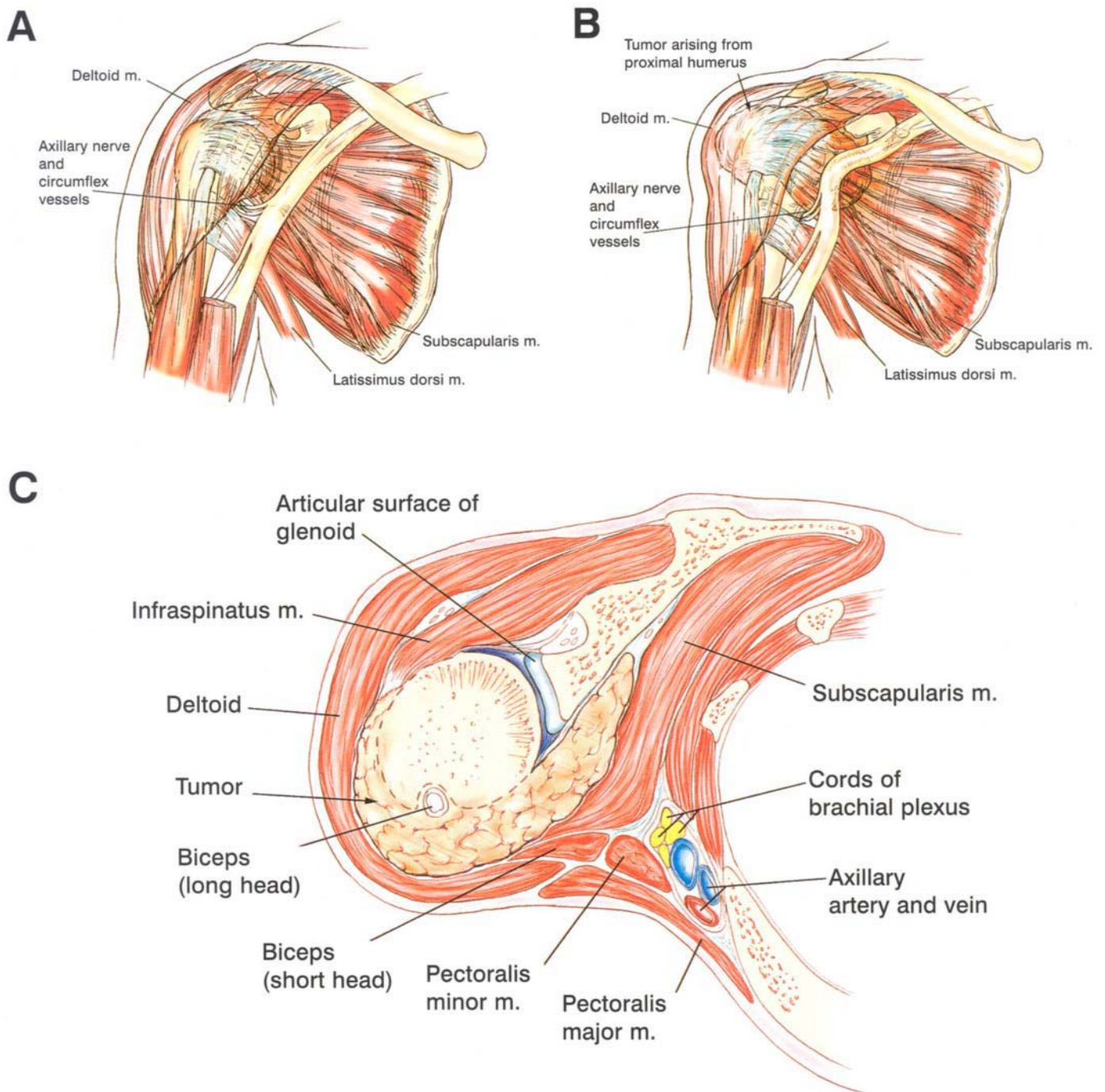
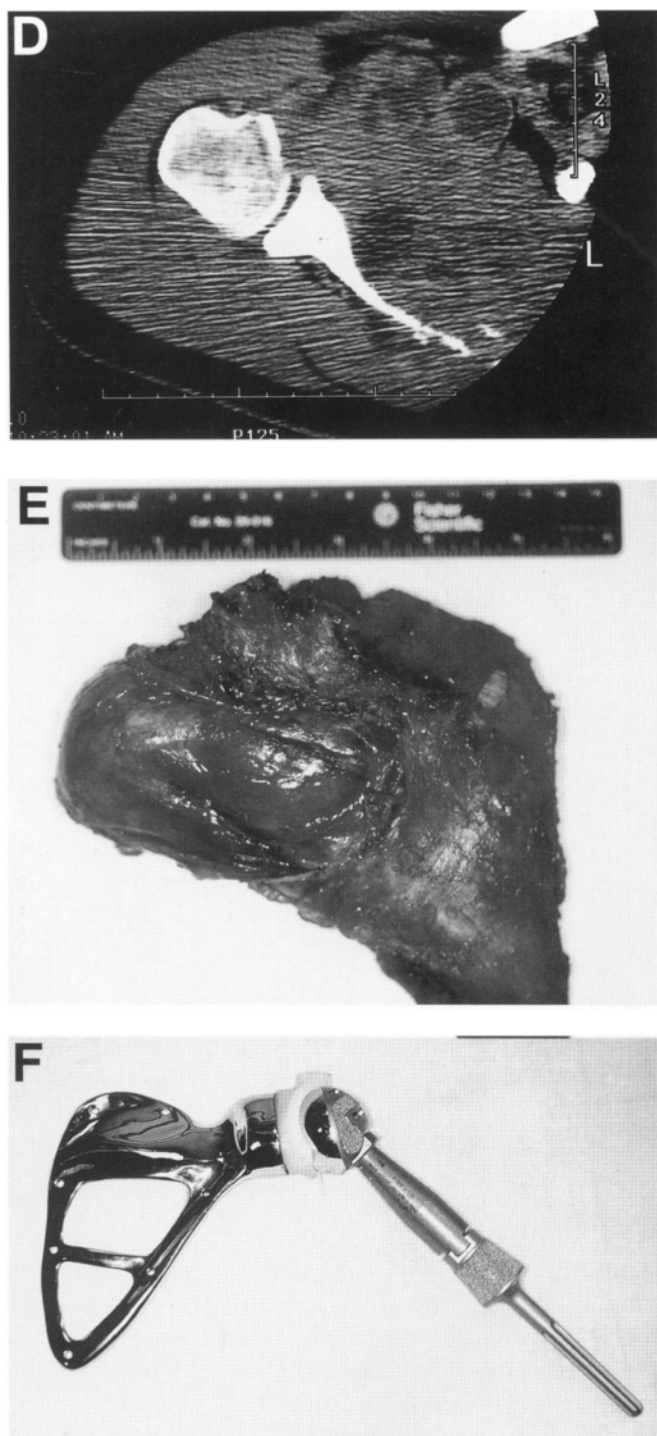


Figure 9.17 (see above and following page). Techniques in shoulder and elbow surgery vol 2 no 1 2001 pp. 54-69.



glenoid and scapular neck also reside within the functional compartment of the proximal humerus since they are contained by the rotator cuff and capsule and the subscapularis muscle. Sarcomas that arise from the proximal humerus and extend beyond the cortices

Figure 9.17 Functional anatomic compartment of the proximal humerus. (A) The proximal humerus is surrounded by the subscapularis and latissimus dorsi anteromedially, the deltoid laterally, and the remaining rotator cuff superiorly and posteriorly. These muscles form a functional anatomic compartment surrounding the proximal humerus. The only neurovascular structures that enter this compartment are the humeral circumflex vessels and the axillary nerve. (B) Schematic showing the local growth of a high-grade spindle cell sarcoma arising from the proximal humerus. High-grade sarcomas most commonly penetrate the bony cortices of the proximal humerus and compress the surrounding muscles into a pseudocapsular layer. The surrounding muscle fascia poses a barrier to tumor extension and contains the tumor within the functional anatomic compartment surrounding the shoulder. The deltoid, subscapularis, and infraspinatus muscles are compressed into a pseudocapsular layer. The glenoid and lateral scapula are also contained within this compartment. High-grade sarcomas grow centripetally and will follow the fascial borders of the compartment to the opposing glenoid surface. (C) Cross-section of the glenohumeral joint demonstrating a high-grade sarcoma arising from the metaphyseal region of the proximal humerus. The deltoid, subscapularis, and infraspinatus muscles contain the tumor. The subscapularis muscle protects the neurovascular structures (i.e. axillary vessels and brachial plexus) from tumor involvement, thus permitting limb-sparing resection in most cases (arrow). Tumors that protrude beyond the bony cortices extend along the capsule and rotator cuff muscles to the opposing glenoid and scapula. (D) CT scan demonstrating marked destruction of a scapula secondary to a Ewing's sarcoma. There is tumor involvement of the glenohumeral joint. A Type IV (Tikhoff–Linberg) resection was performed following induction chemotherapy. (E) Gross specimen showing the scapula covered by its adjacent musculature. (F) A modern scapula prosthesis that can be mated to a proximal humeral component (Howmedica, Inc.) This is a newer design of the scapular prosthesis that has holes along the glenoid as well as the vertebral and axillary borders for reattachment of the shoulder girdle musculature with 3-mm Dacron tape. The capsular mechanism is reconstructed with a Gore-tex® graft.

compress these muscles into a pseudocapsular layer. The fascial layers surrounding these muscles resist tumor penetration. The only neurovascular structures that enter this compartment are the axillary nerve and humeral circumflex vessels. The main neurovascular bundle (brachial plexus and axillary vessels) to the upper extremity passes anterior to the subscapularis and latissimus dorsi muscles. These muscles and their investing fascial layers are therefore particularly important for protecting the neurovascular bundle from

tumor involvement. They also protect the pectoralis major muscle that must be preserved during surgical resection for soft tissue coverage.

High-grade sarcomas that extend beyond the bony cortices of the proximal humerus expand the investing muscles that form the compartmental borders and pseudocapsular layer. They grow along the path of least resistance and therefore are directed toward the glenoid and scapular neck by the rotator cuff and glenohumeral joint capsule. Anteriorly, the tumor is covered by the subscapularis that bulges into and displaces the neurovascular bundle. Only rarely will a very large proximal humerus sarcoma extend beyond the compartmental borders. In these instances the tumor usually protrudes through the rotator interval. A wide (compartmental) resection for a high-grade sarcoma must therefore include the surrounding muscles that form the pseudocapsular layer (deltoid, lateral portions of the rotator cuff), the axillary nerve, humeral circumflex vessels and the glenoid (extra-articular resection of the proximal humerus).

Most high-grade scapular sarcomas arise from the region of the scapular neck. The compartmental borders surrounding the scapula neck consist of the rotator cuff muscles and portions of the teres major and latissimus dorsi muscle. The compartment consists of all of the muscles that originate on the anterior and posterior surfaces of the scapula; the subscapularis, infraspinatus, and teres muscles. The deltoid, although not one of the compartmental borders, since it attaches to a narrow region of the scapular spine and acromion, may be involved secondarily by a large soft-tissue extension. In most instances the deltoid is protected by the rotator cuff muscles because of the anatomic origin of most tumors from the neck region. Similar to the proximal humerus, the rotator cuff muscles are compressed into a pseudocapsular layer by sarcomas that arise from the scapula. The subscapularis also protects the neurovascular bundle from tumor involvement. The head of the proximal humerus is contained within the compartment surrounding the scapula by the rotator cuff muscles. Wide resection of a high-grade scapular sarcoma must therefore include the rotator cuff and, in most instances, the humeral head. The axillary nerve is not contained within the compartment and therefore can be spared from resection. Additionally, because the deltoid is not compressed into a pseudocapsular layer, it can usually be preserved.

Proximal Humerus

Malignant tumors often present with large soft-tissue components (Stage IIB) underneath the deltoid that extend medially and displace the subscapularis and

coracobrachialis muscles.^{16,17} Pericapsular and rotator cuff involvement occurs early and must be evaluated.

Glenohumeral Joint

The shoulder joint appears to be more prone to intra-articular or pericapsular involvement by high-grade bone sarcomas than are other joints. There are several mechanisms for tumor spread: direct capsular extension, tumor extension along the long head of the biceps tendon, fracture hematoma from a pathologic fracture, or poorly planned biopsy. These mechanisms make patients who undergo intra-articular resections for high-grade sarcomas at greater risk for local recurrence than those undergoing extra-articular resections. Therefore, it is often necessary to perform an extra-articular resection for high-grade bone sarcomas of the proximal humerus or scapula.

Neurovascular Bundle

The subclavian artery and vein join the cords of the brachial plexus as they pass underneath the clavicle. Beyond this point the nerves and vessels can be considered as one structure (i.e. the neurovascular bundle). Large tumors involving the upper scapula, clavicle, and proximal humerus may displace the infraclavicular components of the plexus, which may necessitate sacrifice of some of the major nerves.

Musculocutaneous and Axillary Nerves

These two nerves are often in close proximity to or in contact with tumors around the proximal humerus. The musculocutaneous nerve is the first nerve to leave the brachial plexus. It typically leaves the lateral cord just distal to the coracoid process, passes through the coracobrachialis, and runs between the brachialis and biceps. It should be preserved, if possible, to maintain normal elbow function. The path of this nerve may vary extensively (within 6–8 cm of the coracoid). It should be identified prior to any resections because it can be easily injured at any of these locations.

The axillary nerve arises from the posterior cord and courses, along with the circumflex vessels, inferior to the distal border of the subscapularis. It then passes between the teres major and minor to innervate the deltoid muscle posteriorly. Tumors of the proximal humerus are most likely to involve the axillary nerve as it passes adjacent to the inferior aspect of the humeral neck, just distal to the joint. Therefore, the axillary nerve and deltoid are almost always sacrificed when the proximal humerus is resected.

Radial Nerve

The radial nerve comes off the posterior cord of the plexus and continues anterior to the latissimus dorsi and teres major. Just distal to the teres major, the nerve courses into the posterior aspect of the arm to run between the medial and long head of the triceps. Although most sarcomas of the proximal humerus do not involve the radial nerve, it must be isolated and protected prior to resection.

Axillary and Brachial Arteries

The axillary artery is a continuation of the subclavian artery and is called the brachial artery once it passes the inferior border of the axilla. It is surrounded by the three cords of the brachial plexus and is tethered to the proximal humerus by the anterior and posterior circumflex vessels. Early ligation of the circumflex vessels is a key maneuver in resection of proximal humeral sarcomas because it allows the entire distal brachial artery and vein to fall away from the tumor mass. Occasionally, there is anatomic variability in the location of its branches that would lead to difficulty in identification and exploration if not previously recognized. A preoperative angiogram can help determine vascular displacement and anatomic variability.

Scapula (Figure 9.17D–F)

Tumors of the scapula often become quite large before being diagnosed. In their early stages, tumors arising in the body of the scapula are surrounded by a cuff of muscle in all dimensions. Important areas to evaluate are the chest wall, axillary vessels, proximal humerus and rotator cuff, and periscapular tissue.

Glenohumeral Joint

Sarcomas arising from the glenoid or scapular neck usually involve the joint and adjacent capsule. Therefore, an extra-articular resection through both anterior and posterior approaches (see Surgical Techniques section) should be performed for tumors in this location.

Neurovascular Involvement

As sarcomas of the scapula enlarge, they may produce a large axillary component and involve the axillary vessels and brachial plexus. When there is a large anterior extraosseous mass, anterior exploration of the neurovascular bundle should be performed to determine resectability or facilitate an extra-articular resection.

Lymph Nodes

The axillary and supraclavicular lymph nodes should be carefully examined preoperatively. Lymph node biopsy may be necessary to determine resectability.

Suprascapular Tumors

This is a difficult area to evaluate by physical exam and even with modern imaging techniques. Large tumors in this location often extend into the anterior and posterior triangles of the neck, making resection difficult or contraindicated, except for purposes of palliation.

SURGICAL TECHNIQUES

See Chapters 33 and 34 .

ENDOPROSTHETIC RECONSTRUCTION

Endoprosthetic reconstruction was developed in the 1940s (Figure 9.18). Initially, attention focused on reconstruction of skeletal defects of the lower extremity. Use of the technique was gradually broadened to include defects of the upper extremity and shoulder girdle. Marcove¹⁸ and Francis¹⁹ performed some of the first resections for high-grade sarcomas in this location in the late 1960s and 1970s. During the early 1980s all prosthetic replacements were custom-made for each patient. In 1988 a modular replacement system (MRS), that obviates the need for custom devices, was developed by Howmedica, Inc. (Rutherford, NJ) (Figure 9.19).

The MRS has undergone several design changes and improvements since that time. The MRS is used in conjunction with both intra- and extra-articular resections, and results are highly predictable and successful. Reported rates of fracture, infection, nonunion, reoperation, and tumor recurrence are lower, and time of immobilization is shorter with endoprosthetic reconstruction than with allograft, composite reconstruction, or arthrodesis. Survival of the MRS proximal humeral prosthesis is reported to be 95–100% at 10 years (Figure 9.20).²⁰

Design Features: Proximal Humeral Endoprosthesis

1. Modular components, including stem, body, and humeral head.
2. Polished intramedullary stems for cement fixation available in multiple diameters and lengths.
3. Facing reamer to create a perfect "seat" for the stem–bone interface that protects the stem from bending stresses.

4. Porous coating (circumferential) at the prosthesis–bone junction for ingrowth of extracortical bone graft and soft tissue to seal the bone–cement–stem interface. Incorporation of extracortical bone graft also protects the prosthetic stem by sharing bending and loading stresses.
5. Humeral heads (available in two sizes) with porous coating and metal loops or holes to facilitate muscle and tendon attachment and soft-tissue ingrowth.

Design Features: Scapular Replacement Prosthesis

1. Nonconstrained or semiconstrained design.
2. Holes along the periphery of the prosthetic scapular body for reattachment of the scapular stabilizing muscles (levator scapulae, rhomboids, and trapezius muscles).
3. Holes along the base of the prosthetic scapular neck for capsular reconstruction with native capsule or Gore-Tex aortic graft.

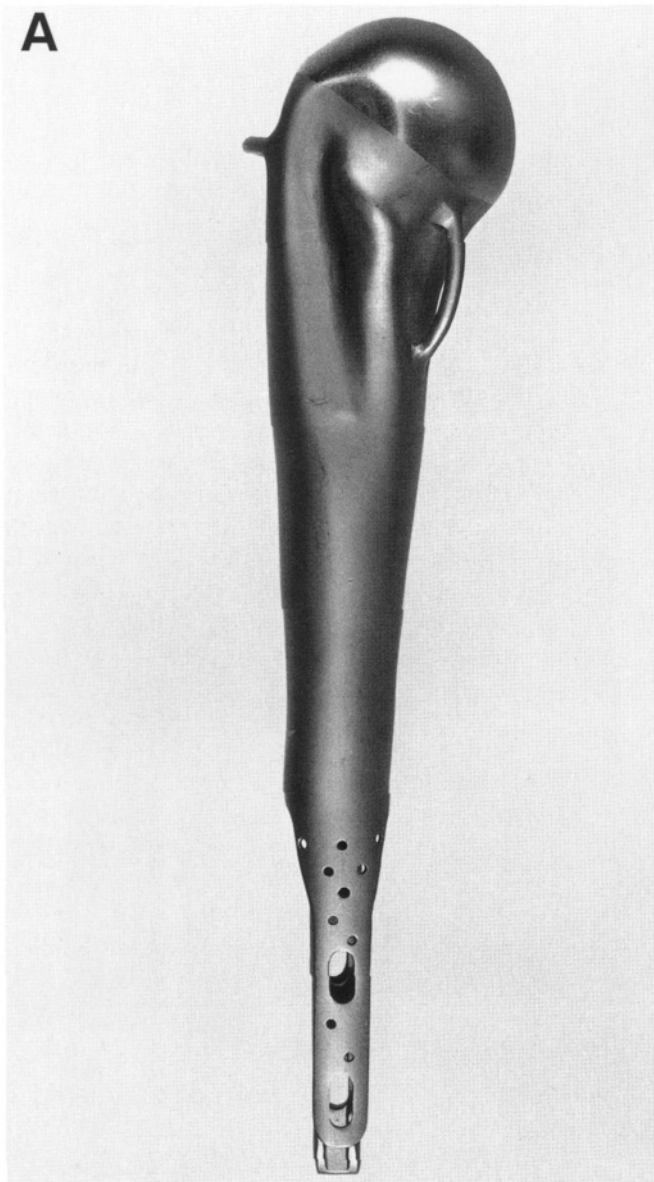


Figure 9.18 (A) The original custom prosthesis utilized during the 1960s as developed by Howmedica, Inc. (B) Plain radiograph of the proximal humerus modular replacement system that has been in use in the United States since 1988. A modular system consists of three components: the head, body, and stem.



FUNCTIONAL AND REHABILITATION CONSIDERATIONS

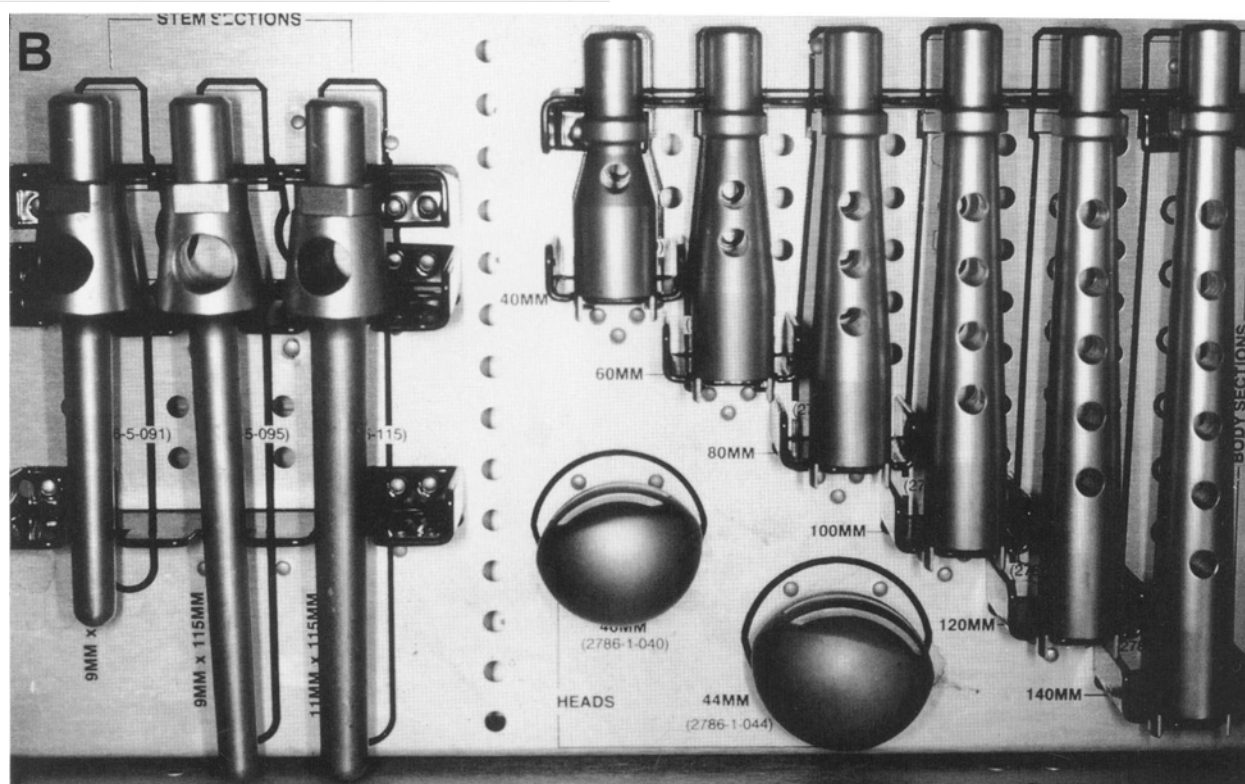
Patients undergoing shoulder girdle resections retain hand and elbow function, but lose shoulder motion. The goal of shoulder girdle reconstructions is to provide a stable shoulder that allows positioning of the arm and hand in space, thereby preserving function. The functional and cosmetic outcome is superior to that of a forequarter amputation.

Proximal Humeral Resections

Function

The goal is to obtain a stable shoulder girdle with preservation of full elbow, wrist, and hand function. Shoulder stability is obtained by multiple muscle transfers and reconstruction. Shoulder motion is dependent upon the type of resection required (Type I or V) and the preserved soft tissues. Some shoulder motion is expected, but shoulder abduction is usually extremely limited unless the axillary nerve and deltoid muscle have been preserved. Most patients regain full

Figure 9.19 (A) Modular replacement system showing the various sizes for the proximal humerus. (B) The large holes within the body and the stems indicate these components are trial components.



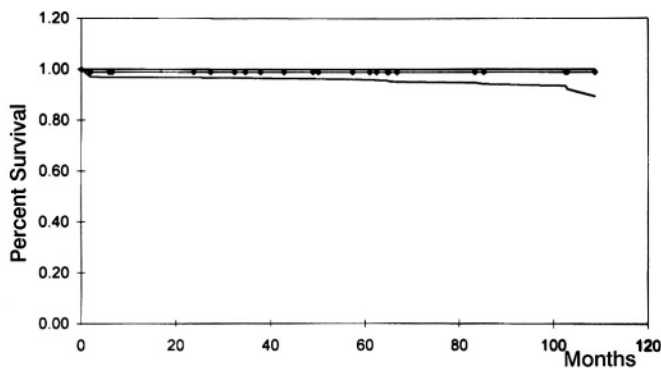


Figure 9.20 Kaplan-Meier curve of 23 proximal humeral prostheses performed for reconstruction following extra-articular resection (Type V) for high-grade osteosarcomas. There has been no prosthetic loosening and the actuarial prosthetic survival rate is 100% at 100 months.

internal and external rotation, flexion and extension of 30–50 degrees, and 10–30 degrees of active abduction.

Patients who undergo proximal humeral resections generally regain normal elbow and hand function.

Rehabilitation

The rehabilitation process begins with a preoperative patient orientation program that often gives the patient the opportunity to meet someone who has undergone a similar procedure, to discuss the perioperative course and demonstrate the expected functional and cosmetic outcome.

A sling is applied in the operating room to provide shoulder and arm support and restrict motion. Edema is controlled with elevation and a compression wrap or stocking. In the immediate postoperative period the patient is instructed on motion exercises for the wrist and hand, and elbow flexion is encouraged within the confines of the sling. Neck motion and shoulder elevation exercises are instituted within 1–2 days following surgery.

Once the incision has healed and the sutures are removed, at 2–4 weeks after surgery, shoulder exercises and elbow extension are begun. Pendulum exercises and gentle shoulder motion (flexion, extension, internal and external rotation) are done with the help of a family member or physical therapist. Elbow flexion, extension, supination and pronation are also performed. The sling is removed for therapy but is subsequently reapplied to provide support until shoulder girdle stability and arm strength are improved. Gentle strengthening is instituted once motion has returned, with the use of active motion and isometric exercises and light weights (2–10 pounds).

Normal daily activities are encouraged, but weights in excess of 20 pounds should not be lifted with the reconstructed extremity.

Total Humeral Resections

The unique postoperative considerations following total humeral replacement are the potential for arterial occlusion or thrombus and nerve compression or neuropraxia. Postoperative edema may be more severe and may require a compressive stocking for control. A sling is required for a longer period of time than following proximal humeral resections to allow for healing of the soft tissue of the shoulder girdle and elbow joint. Fortunately, for true diaphyseal tumors, most of the musculature about the shoulder girdle and elbow can be preserved, thereby allowing shoulder stability and normal elbow function.

Scapular Resections

Function

There is minimal functional loss following partial scapular resections (Type II), shoulder motion and strength are almost normal. Total scapular resections (Types III and IV) result in significant loss of shoulder motion, predominantly shoulder abduction. If a prosthesis is utilized, abduction to 60–90° can be obtained. Elbow and hand function should be normal, again depending on the extent of the resection and remaining nerves. Soft-tissue reconstruction is the key to establishing shoulder stability and obviating the need for an external orthosis.

Rehabilitation

A sling is required for approximately 2–4 weeks to allow healing of the transferred muscles, which provide the stabilizing force to the upper extremity. A compression arm stocking may be required to prevent swelling in the immediate postoperative period. Motion of the hand and wrist, and elbow flexion, are encouraged in the immediate postoperative period. Elbow extension and shoulder motion are initiated after the incision has healed, approximately 2–4 weeks after surgery. Gentle motor strengthening is begun approximately 6 weeks after surgery, with the goal of strengthening the pectoralis major, latissimus dorsi, trapezius, and other scapular stabilizers. Cosmetic appearance is markedly improved following prosthetic replacement of the scapula compared to those patients left without a scapula reconstruction. In addition, abduction and external rotation is partially restored.

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10

Overview of Pelvic Resections: Surgical Considerations and Classification

Jacob Bickels and Martin Malawer

OVERVIEW

The bony pelvis and its enveloping soft tissues are a common site for bone and soft-tissue tumors. Extensive pelvic surgeries, either for oncologic reasons or following trauma, are highly demanding because of the irregular and complex shape of the bony pelvis, numerous muscle attachments, and the proximity of major blood vessels, nerves, and visceral organs (Figure 10.1).

Until the late 1970s most pelvic tumors were treated with hemipelvectomy, a procedure that was associated with a significant percentage of complications and a dismal functional and psychological outcome. Because of the availability of more accurate modalities for imaging of the pelvis, use of neoadjuvant chemotherapy, improved resection techniques, and prosthetic reconstruction, limb-sparing procedures are now performed in the majority of these cases. An important consideration, because of the use of adjuvant chemotherapy and, occasionally, radiation therapy, is that the patient's postoperative recovery period be short and uncomplicated. This chapter discusses specific anatomic and clinical considerations, related to surgery in the pelvic area, as well as the various classifications of pelvic resections.

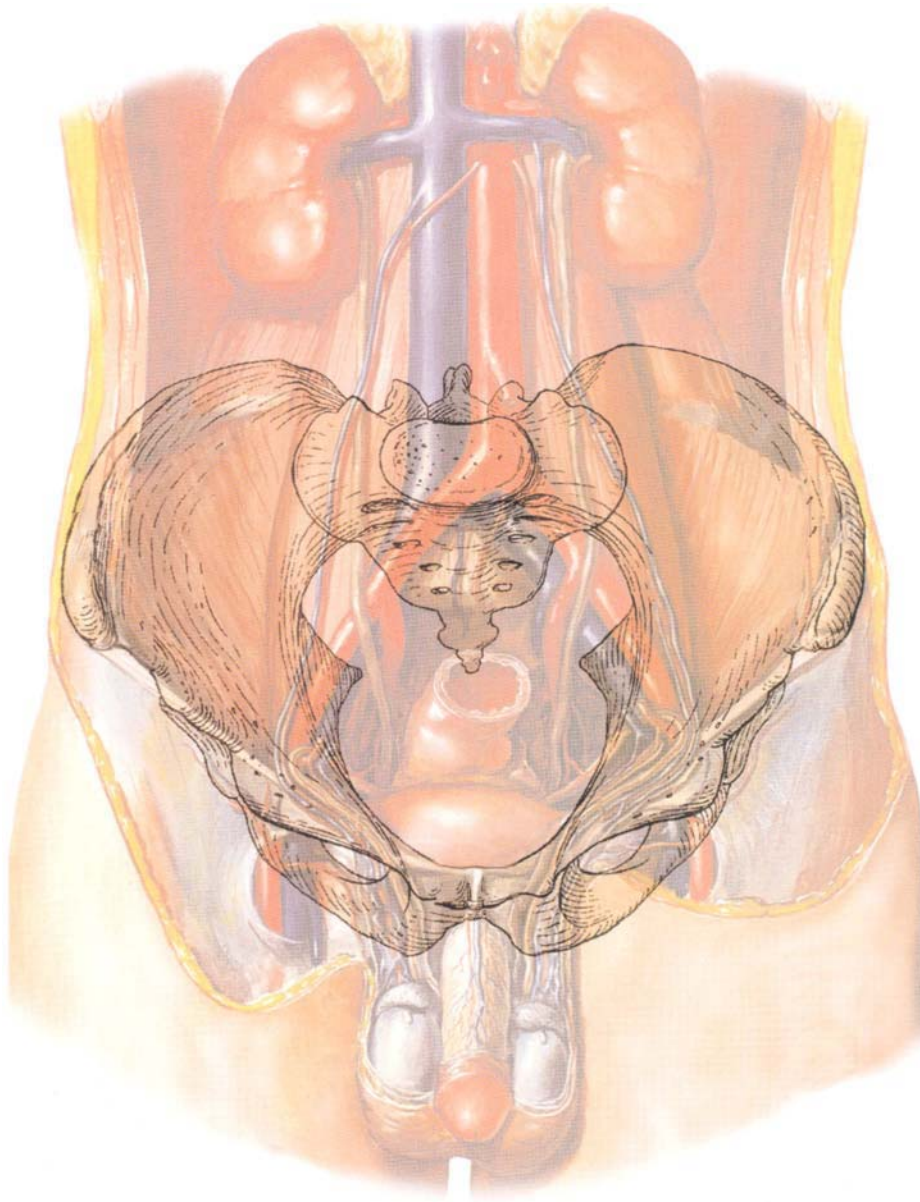


Figure 10.1 The bony pelvis and its relation to the major blood vessels, nerves, and visceral organs

INTRODUCTION

Lesions in the pelvis usually attain considerable size before they are diagnosed. Most patients with lesions of the iliac crest that extend into the pelvis, or lesions that arise in the pelvic fossa, complain initially of vague abdominal pain or fullness. Patients may present with symptoms that are related to pressure on a specific anatomic structure within the pelvis. Rarely do patients present with systemic signs of advanced malignancy. Occasionally, a large, asymptomatic mass is felt on abdominal or pelvic examination.

In most cases a wide excision of a pelvic or proximal thigh tumor may be performed without compromising any vital structure of the lower extremity. Hemipelvectomy is indicated in cases where a severe compromise following wide excision is inevitable. A functionally impaired lower extremity is preferable to an amputation, and even patients whose sciatic or femoral nerves have to be sacrificed do well with proper training, orthoses, and physical therapy. A local recurrence of a previously resected soft-tissue or bone sarcoma is no longer a clear indication for an amputation, because its impact on survival is questionable. Local

recurrences are, therefore, treated with wide excision, and amputations are performed with the same indications as for primary tumors.

IMAGING OF THE PELVIS

Staging studies for pelvic lesions, as for those elsewhere in the musculoskeletal system, are aimed at determining local tumor extent, its relation to the specific anatomic structures within the pelvis, and the presence of metastatic disease. The combination of these findings, along with the histopathologic diagnosis, will determine whether surgery is indicated and, if so, to what extent. The extent of a pelvic tumor can be evaluated only by combining multiple imaging modalities, and even then the full extent of most tumors is underestimated (Figure 10.2).

Plain Radiography

Plain radiography is of limited value in the assessment of pelvic girdle lesions. The images are frequently obscure and confusing. The pelvis, and particularly the sacrum, is a difficult structure in which to recognize early bone lesions because of the almost universal presence of overlying intestinal gas. Many lesions are overlooked initially. For these reasons there should be a low threshold for performing computed tomography (CT), magnetic resonance imaging (MRI), or bone scan

in patients presenting with deep pain around the pelvic girdle or an atypical pattern of sciatic pain (Figure 10.3).

CT and MRI

Contrast CT is the key modality for assessment of bony lesions of the pelvic girdle. The extent of bone destruction, cortical breakthrough, characteristics of the tumor matrix, and reactive changes in the host bone and soft tissues can be determined. MRI is used to evaluate soft-tissue tumors and the extent of medullary and extraosseous components of bone tumors. It is accurate within approximately 1 cm of the tumor margin. A notable exception is chondrosarcoma, which is typically understaged when it occurs in the pelvis. CT was shown to underestimate their size by up to 40–50% (Figure 10.4). Great caution should therefore be used in the surgical planning of resection of these tumors. It is also important to note that chondrosarcoma is the most common primary bone sarcoma of the pelvic girdle. Any chondroid-containing tumor of the pelvis is extremely likely to be a chondrosarcoma, and any diagnosis of an enchondroma should be seriously questioned.

Angiography

Angiographic studies are valuable in evaluating the relation of the major blood vessels to a tumor, their patency, as well as assessing tumor vascularity. These

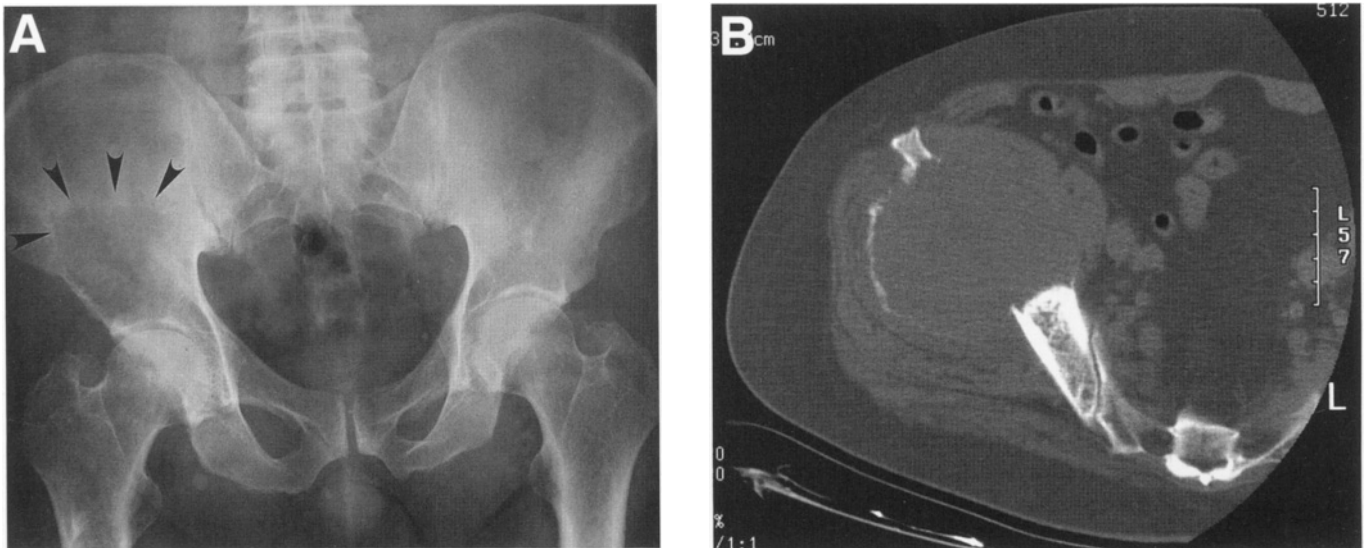


Figure 10.2 A 75-year-old patient with a 1-year history of right hip pain. Past medical history includes a subtotal thyroidectomy that was performed for an unclear diagnosis. The patient was told that the lesion was benign, and no further treatment was indicated. The patient was referred for total hip replacement and plain radiographs revealed a large lytic lesion of the right periacetabular region (A – arrows). On the basis of this radiograph one might assume that the cortices are intact. (B) CT showed extensive bone destruction and extension of the tumor to the pelvis and the right gluteal region. Complete staging demonstrated two lung metastases, and CT-guided core needle biopsy revealed a metastatic thyroid carcinoma. Following preoperative embolization the patient was treated with resection–curettage (curettage and meticulous burr drilling) and cementation.

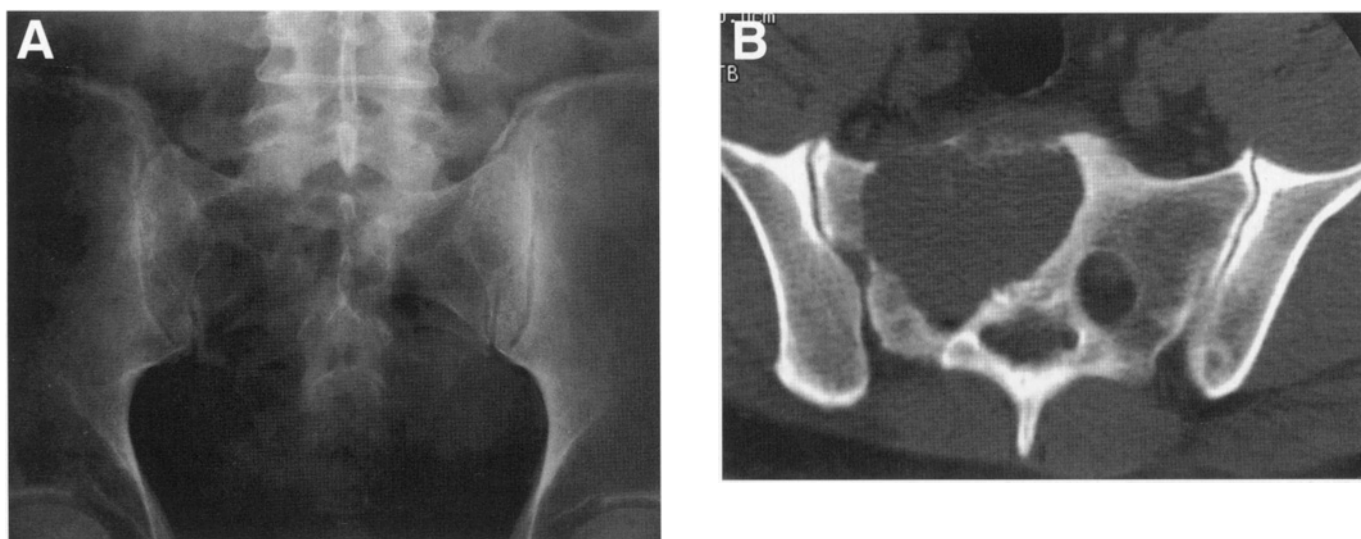


Figure 10.3 A 55-year-old male with a low back and posterior thigh pain. (A) Anteroposterior plain radiograph of the pelvis was read as normal. (B) CT of the pelvis revealed a large destructive lesion of the sacrum. CT of the abdomen revealed a renal mass, and a CT-guided core needle biopsy of the sacral lesion confirmed the diagnosis of metastatic hypernephroma. Complete staging revealed additional asymptomatic vertebral metastases. The patient was treated with embolization of the sacral lesion with complete resolution of his pain.

data are crucial in planning the resection of deep-seated pelvic tumors, especially large tumors that may displace the major blood vessels. These tumors occasionally form mural neoplastic thrombi, the presence of which must be confirmed prior to surgery. In addition, reduction in tumor vascularity, as revealed by serial angiographs, was shown to be indicative of good response to preoperative chemotherapy. Embolization of highly vascularized lesions, e.g. metastatic hypernephromas, can significantly reduce tumor size, blood loss in surgery, and alleviate symptoms in patients who are not candidates for surgery (Figures 10.5 and 10.6).

ANATOMIC CONSIDERATIONS

Evaluation of the full anatomic extent of a pelvic tumor cannot be based on a single imaging modality. Combined data, gained from two or more imaging modalities, allow a realistic appreciation of the exact anatomic extent. Even when that information is available, however, the full extent of a pelvic tumor is commonly underestimated preoperatively. The review of any imaging study of the pelvis, because of the numerous anatomic details, must be performed very methodically. The authors review the structures from the back (midsacral region) and follow the pelvic girdle to the front (symphysis pubis), as described in the following paragraphs.

1. *Sacrum, sacral alae, and sacroiliac joint.* Most patients who undergo extended hemipelvectomy, which

necessitates transection of the sacrum through the ipsilateral neural foramina, regain function of the gastrointestinal and genitourinary tracts. Adding a contralateral compromise of the sacral nerve root will create a severe dysfunction. Tumors that penetrate the sacrum and cross the midline are considered, therefore, unresectable because of the involvement of bilateral nerve roots (Figure 10.7). The tumor can be resected, but the morbidity will outweigh the questionable oncologic benefit from surgery.

The common iliac vessels are just anterior to the sacral ala, and any cortical breakthrough by a tumor in that site may be expected to extend directly to the blood vessels. The sacroiliac (SI) joint is a key anatomic landmark. The major nerves and blood vessels are medial to it: therefore, any tumor or pelvic resection that is lateral to the SI joint is expected not to violate the major neurovascular bundle. Involvement of the SI joint must be documented prior to surgery by using the combination of CT, MRI, and bone scan.

2. *Major pelvic blood vessels and structures.* The common iliac artery bifurcates along the sacral ala, and the ureter crosses the bifurcation in each side. Large tumors around the sacral ala frequently displace and occasionally invade these structures. The mere presence of a major blood vessel or a pelvic viscus involvement is not an indicator of unresectability. If curative resection is planned, both structures can be excised en-bloc with the tumor and be repaired with a graft. However, when a compound resection (bony

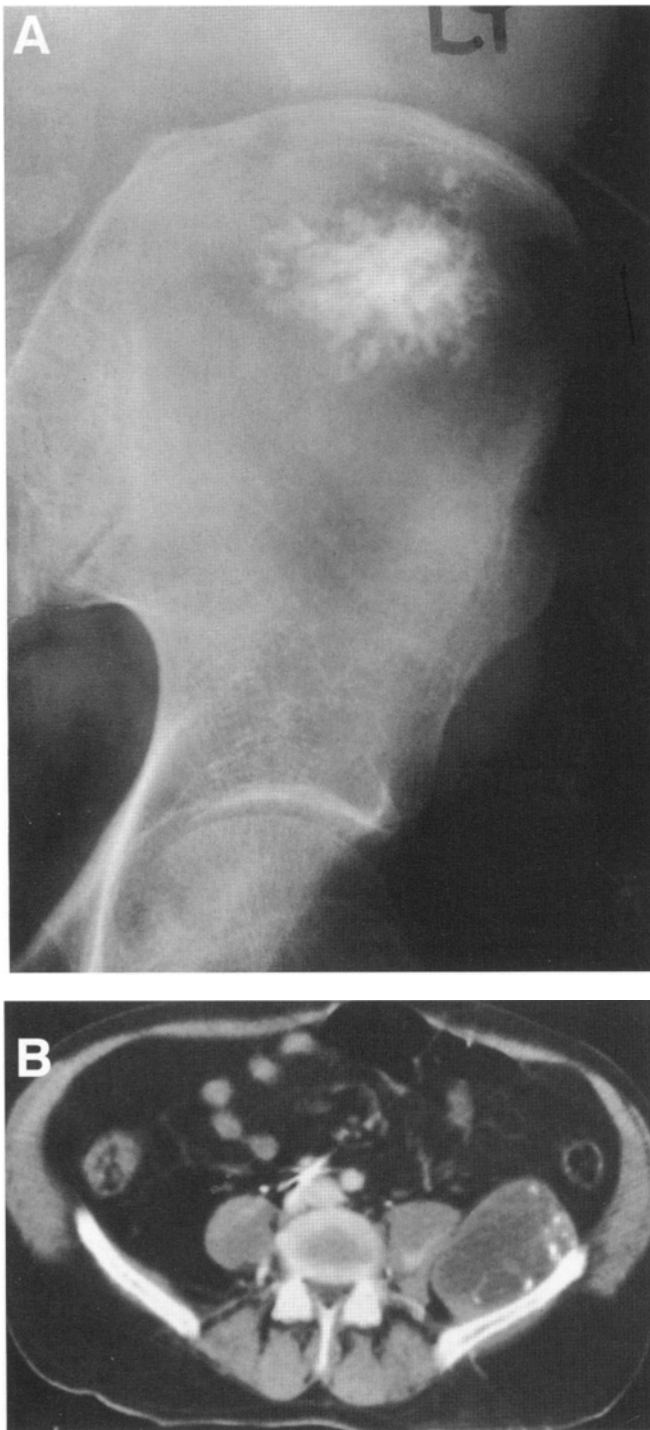


Figure 10.4 A 44-year-old patient presented with left flank pain. (A) Plain radiographs revealed a cartilage-forming lesion in the left ilium. On the basis of that study alone it seemed that this was an intraosseous lesion. (B) CT showed an extensive tumor on the medial aspect of the ilium with destruction of the inner table and extension to the pelvis. CT-guided core needle biopsy showed intermediate- to high-grade chondrosarcoma and the patient underwent en-bloc resection of the ilium with the large extraosseous component. (Cancer: Principles and Practice of Oncology, 5th Edition, 1997 38.3:1789–1852)

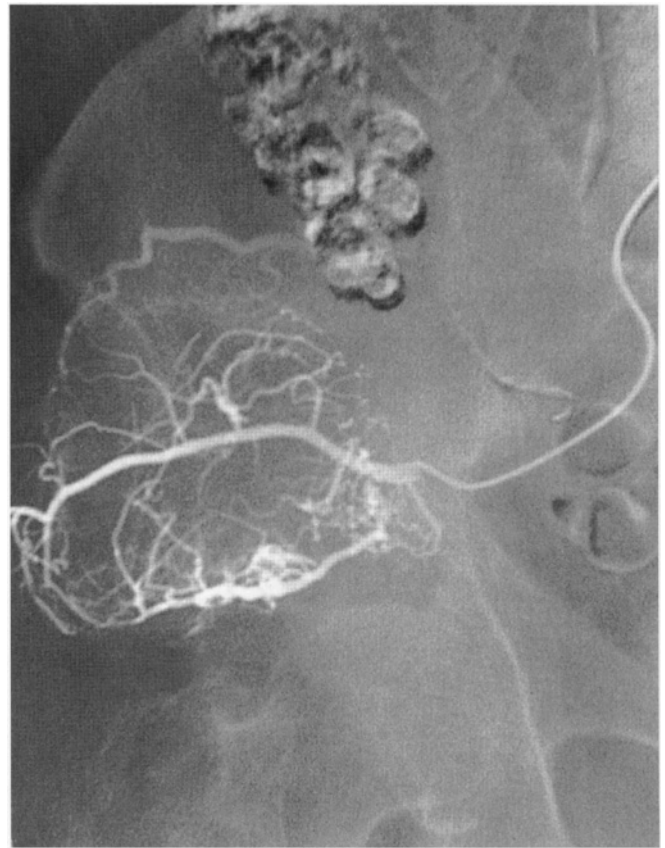


Figure 10.5 Preoperative angiography and embolization of the metastatic lesion, shown in Figures 10.2A and 10.2B. Embolization of a vascular lesion, performed at least 6 h prior to surgery, is expected to significantly reduce intraoperative blood loss.

- pelvis and viscus resection) is anticipated, the patient has to be informed and the surgical assistance and necessary equipment have to be prepared in advance.
3. *Sacral plexus.* Current imaging techniques cannot accurately identify nerves. Nerve involvement is therefore assumed on the basis of the pain pattern, physical examination, and the presence of the tumor in close proximity to a site in which a major nerve or plexus is usually located. Clinical evidence of femoral or sciatic nerve dysfunction usually means direct tumor involvement. In most cases the presence and extent of nerve involvement is established only in surgery. Sacral plexus invasion by tumor has the same significance in terms of resectability as tumor invasion of the sacrum; bilateral involvement is an indicator of unresectability.
 4. *Sciatic notch and nerve.* The sciatic notch is the site of pelvic osteotomy in resections of the ilium or peri-

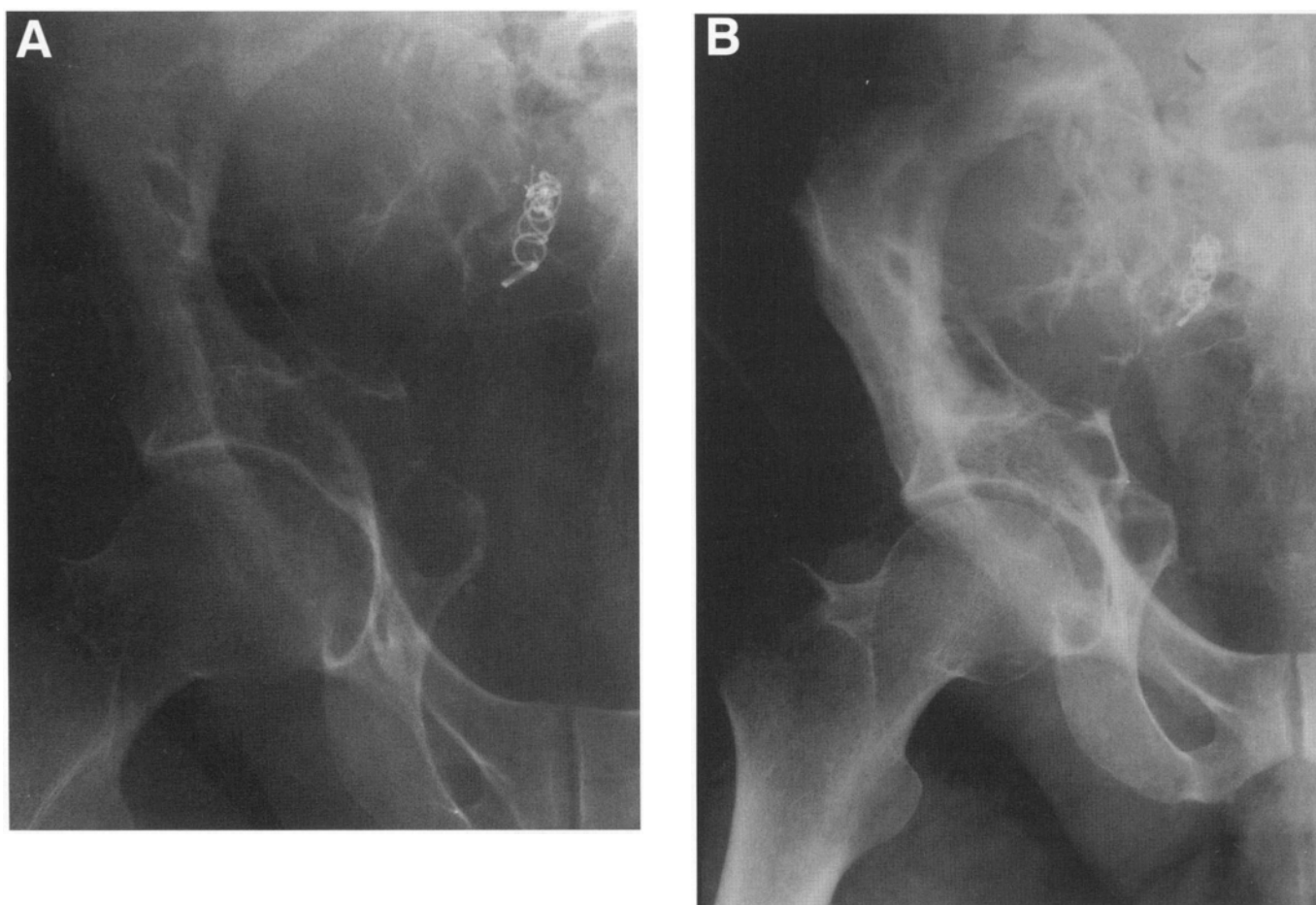


Figure 10.6 A 45-year-old patient presented with excruciating right flank and sciatic pain. Plain radiographs revealed a large destructive lytic lesion of the innominate bone, and staging studies revealed a right renal mass and showed that the sacral lesion crossed the midline to the contralateral sacral foramina. The significance of that finding is that even extended hemipelvectomy would not achieve tumor-free surgical margin. CT-guided core needle biopsy of the sacral lesion established the diagnosis of metastatic hypernephroma and embolization was performed with near-complete resolution of pain after 36 hours. (A) Plain radiograph, performed 24 hours after the procedure (note the coil); and (B) after 6 weeks. Note the thick sclerotic rim of bone in the periphery of the lesion, which is the response of the host bone and indirect evidence of a significant decrease in tumor progression.

acetabular region and in modified hemipelvectomy. CT establishes tumor extension to the sciatic notch, a tight space through which the sciatic nerve and superior gluteal vessels and nerve pass (Figure 10.8). The piriformis muscle, which divides the sciatic notch, is a key structure because the sciatic nerve exits the pelvis underneath it and the superior gluteal artery exits the pelvis above it. The patency of the superior and inferior gluteal arteries, which supply the gluteal vasculature, is established by angiography. Adequate blood supply of the gluteal region is a major consideration in flap design and the gluteal arteries have to be preserved in any pelvic resection, if oncologically feasible. The

superior gluteal artery is located only a few millimeters from the periosteum of the sciatic notch roof, and it should be dissected carefully.

5. *Ilium*. The inner aspect of the bone is covered by the iliacus muscle, which originates from the iliac crest. The iliacus is "pushed" by a growing bone sarcoma and serves as a barrier to direct extension of tumor to the anatomic structures of the pelvis. The iliacus can therefore be used as a safe oncologic margin for resection. In contrast, metastatic carcinomas to the pelvis tend to invade the covering muscle layer in their early growth stage, and a surgical plane between the tumor and near structures cannot be easily defined (Figures 10.9 and 10.10). Although any

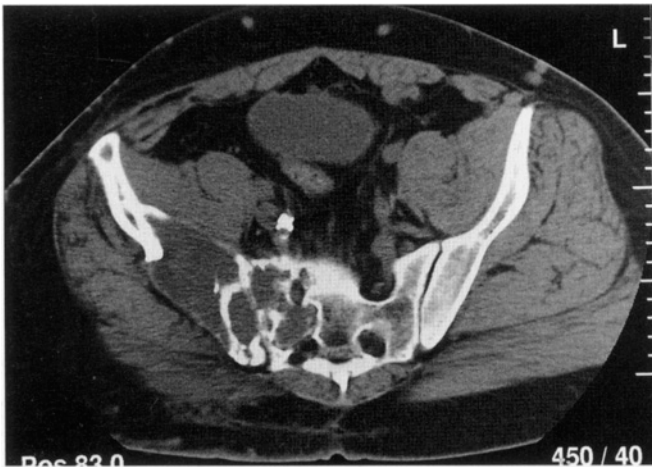


Figure 10.7 High-grade chondrosarcoma of the right sacrum, ilium, and periacetabular region, encasing the ipsilateral sacral foramina. Wide excision would necessitate resection through the contralateral sacral foramina, resulting in an unacceptable functional impairment.

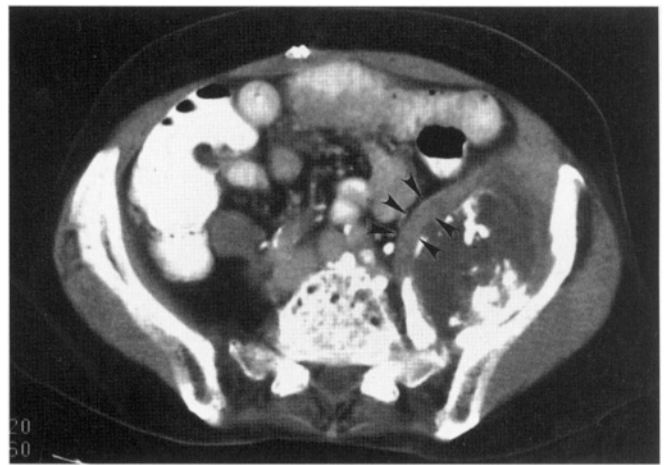


Figure 10.9 The iliacus muscle (arrows) is "pushed" by a growing bone sarcoma and serves as a barrier to direct extension of the tumor to the pelvic viscera. High-grade sarcoma of the left ilium "pushing" the iliacus muscle (arrows) towards the midline.

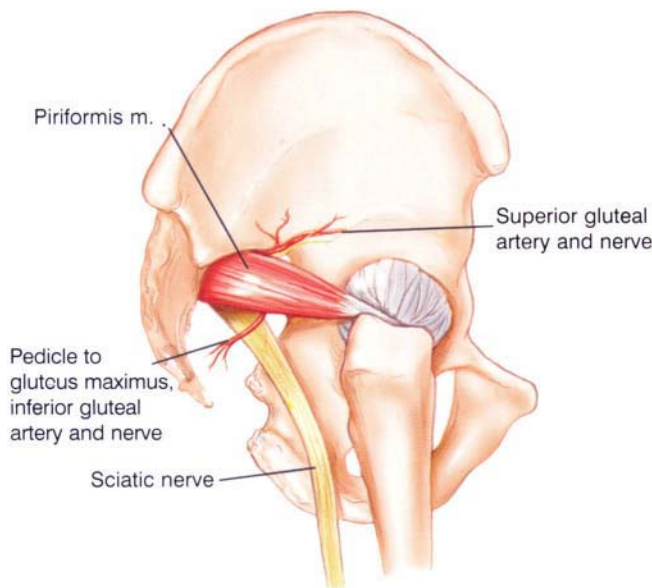


Figure 10.8 The sciatic notch is a tight space through which the sciatic nerve and superior and inferior gluteal vessels and nerves pass. The sciatic nerve exits the notch underneath the piriformis muscle and the superior gluteal vessels exit the notch above it.

pelvic organ can be infiltrated by a tumor, structures that are anterior and posterior to the flare of the muscle (i.e. sacral plexus, sciatic notch and nerve, femoral vessels and nerve, bladder, and prostate) are at a greater risk of direct tumor extension.

6. *Extension to pelvic viscera.* Direct involvement of a pelvic viscus by a pelvic girdle tumor is rare. Left-sided tumors are more likely to involve a component

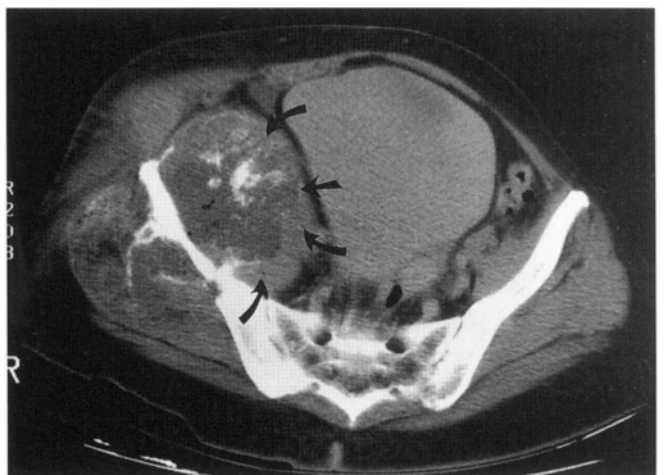


Figure 10.10 Metastatic carcinomas (arrows) to the pelvis tend to invade the covering muscle layer.

of the gastrointestinal tract because of its close proximity to the pelvic girdle at that point. A rectal tube is inserted preoperatively during any pelvic resection to facilitate identification of the rectum during dissection.

7. *Acetabulum and hip joint.* Wide resection of any bone tumor in the periacetabular region, unlike a resection of the ilium or the pubis, imposes a major impairment on the function of the hip joint. It usually necessitates en-bloc resection of the proximal femur and a complex prosthetic reconstruction.
8. *Pubis.* The neurovascular bundle passes just anterior to the superior pubic ramus, and tumors extending to or arising from the pubic ramus are close to the femoral artery, vein, and nerve. In addition, the

urethra passes straight underneath the symphysis pubis. Vulnerable structures such as a major blood vessel, nerve, or a viscus must be identified and mobilized prior to resection. Doing that, the surgeon does not have to assume that these structures are remote and dissection is, therefore, safe; he *knows* that. Establishing the relation of these vulnerable structures to the tumor allows the surgeon to decide whether to proceed with a limb-sparing procedure or perform an amputation, make the necessary preparations for a vascular graft (if needed), and perform a safer resection.

CLASSIFICATION OF PELVIC RESECTIONS

Hindquarter amputation (hemipelvectomy, classical hemipelvectomy), using a posterior subcutaneous flap, was for a few decades the standard of treatment for large bone or soft-tissue tumors involving the proximal thigh, groin, or the periacetabular region. *Extended hemipelvectomy* includes sacral transection through the neural foramina (Figure 10.11). If a part of the iliac crest is spared, the procedure is referred to as *modified hemipelvectomy* (Figure 10.12). Hemipelvectomy can be performed using either the standard *posterior* or *anterior* myocutaneous flaps. If the tumor mass is located in the buttock or high in the posterior thigh, and does not involve the femoral vessels, an anterior flap hemipelvectomy should be performed. In this procedure the surgical defect created by resection of the hemipelvis is covered by a rectus femoris myocutaneous flap. Resection of a viscus in addition to any pelvic girdle specimen is termed *compound hemipelvectomy*.

Internal hemipelvectomy involves resection of part or all of the innominate bone with preservation of the extremity. The classification of these resections is attributed to Enneking¹ and is based on the resected region of the innominate bone, from posterior to anterior: *Type 1* (ilium – Figure 10.13); *Type 2* (periacetabular region – Figure 10.14); and *Type 3* (pubis – Figure 10.15). En-bloc resection of the ilium and sacral ala is classified as an extended *Type 1* or *Type 4* resection.

THE UTILITARIAN PELVIC INCISION

The most useful approach to pelvic biopsy or resection is the utilitarian pelvic incision. All or part of the incision can be used for adequate exploration and resection of the majority of pelvic girdle tumors.

The incision begins at the posterior inferior iliac spine and extends along the iliac crest to the anterior superior iliac spine (Figure 10.16). It is separated into two arms: one is carried along the inguinal ligament up to the



Figure 10.11 Extended hemipelvectomy. Transection is performed through the neural foramina.



Figure 10.12 Modified hemipelvectomy. Transection is performed lateral to the sacroiliac joint. Ipsilateral sacral foramina are, therefore, spared.

symphysis pubis, and the other turns distally over the anterior thigh for one-third the length of the thigh and then curves laterally just posterior to the shaft of the femur below the greater trochanter and follows the insertion of the gluteus maximus muscle. Reflection of the posterior gluteus maximus flap exposes the proximal third of the femur, the sciatic notch, the sacrotuberous and sacrospinous ligaments, the origin of the

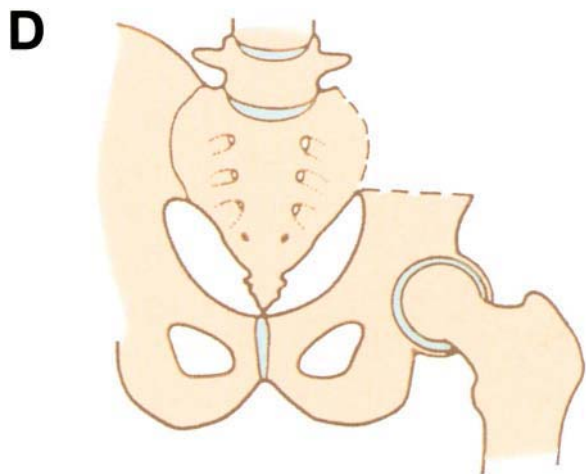
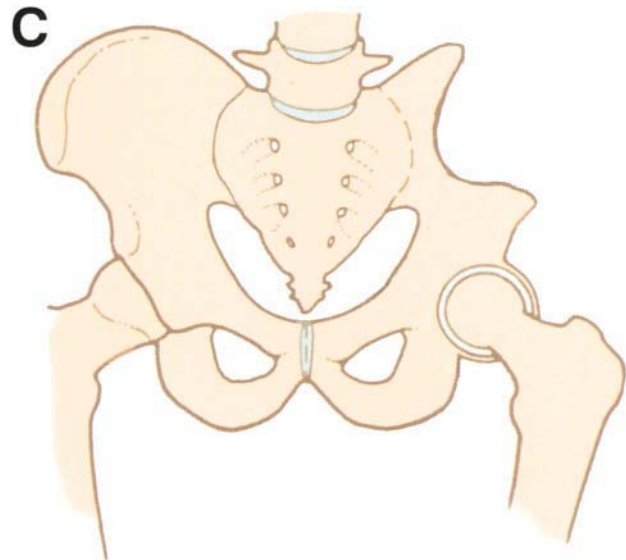


Figure 10.13 Type I pelvic (ilium) resection can be either (A) partial, in which only part of the ilium is transected, or (B) complete. (C,D) An illustration of partial and complete Type I resections, respectively.

hamstrings from the ischium, the lateral margin of the sacrum, and the entire buttock.

A significant concern exists regarding the possible extracompartmental implantation of tumor cells following biopsy or resection of a pelvic tumor, procedures that are difficult to perform under optimal hemostatic

conditions. Unnecessary biopsies must therefore be avoided. If biopsy is indicated, the proper technique and a suitable approach must be chosen. The biopsy tract has to be positioned along the line of the future utilitarian incision, remote from the major neurovascular bundle and the abductors. CT-guided core needle biopsy is considered to be an accurate and safe diagnostic tool in the diagnosis of musculoskeletal tumors and is the preferred modality used by the authors. Guidelines for performing a biopsy were presented in Chapter 2.

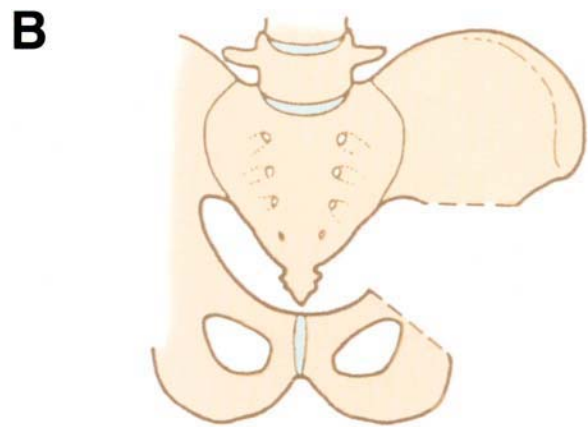


Figure 10.14 (A) Type II pelvic (periacetabular) and Type III resection. Reconstruction was performed with a saddle prosthesis. (B) An illustration of Type II pelvic resection.

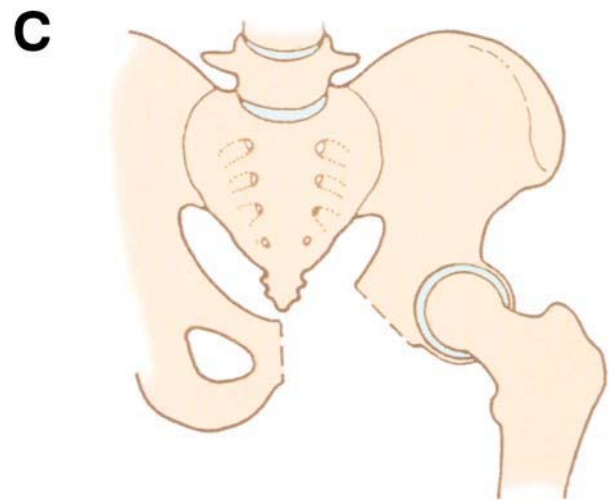
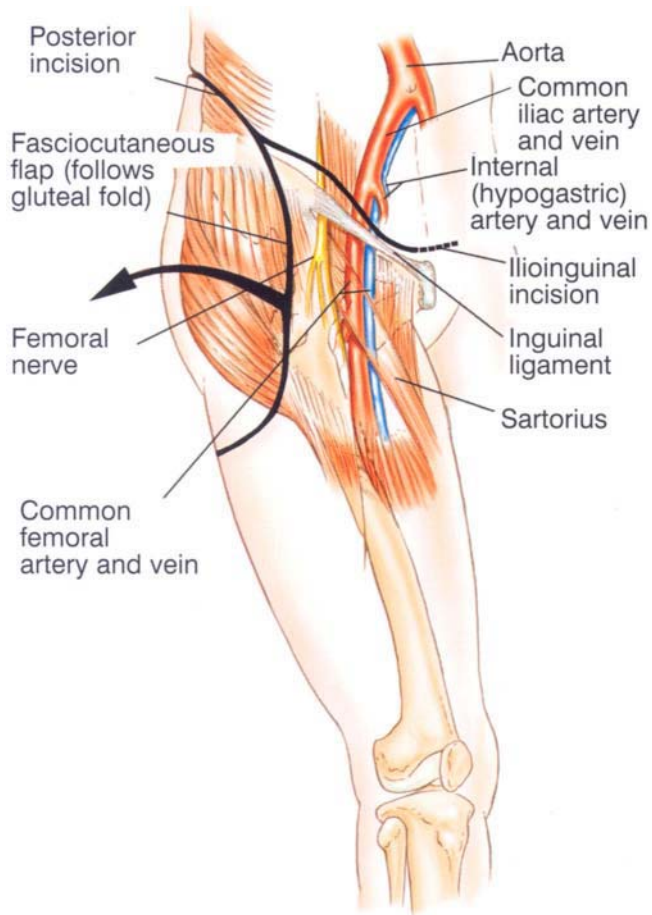


Figure 10.15 Type III pelvic (pubic) resection. These resections may include the (A) superior pubic ramus, inferior pubic ramus, or (B) both rami. (C) An illustration of Type III pelvic resection.



The utilitarian incision may be used for hemipelvectomy by continuing the distal portion of the primary incision posteriorly around and behind the thigh and bringing it anteriorly along the inferior pubic ramus to the symphysis, thus encircling the thigh but still allowing the large posterior flap to be used for primary wound closure.

Figure 10.16 The utilitarian pelvic incision.

Reference

1. Enneking WF. The anatomic considerations in tumor surgery: pelvis. In: Enneking WF, editor. *Musculoskeletal Tumor Surgery*, Vol. 2. New York: Churchill Livingstone; 1983:483–529.

11

Treatment of Metastatic Bone Disease

Martin Malawer

OVERVIEW

Few skeletal metastases require surgical intervention. Radiotherapy, chemotherapy or both often provide symptomatic relief. An impending or actual pathologic fracture requires operative fixation because fractures through a tumor-bearing bone rarely heal without such intervention.

The goals of fixation are to relieve pain, improve function and ambulation, facilitate medical and nursing care, and improve psychological well-being (Figures 11.1 and 11.2). The primary functional goal of surgical intervention is to allow immediate weight-bearing. Surgery should be avoided if this cannot be achieved. A variety of techniques, including prosthetic reconstruction (especially about the hip) or a combination of internal fixation combined with polymethyl methacrylate (PMMA), provides immediate fixation and stability. After the wound has healed, radiotherapy is usually used to arrest local tumor growth, permit bony repair, and prevent re-growth of tumor around the fixation device. This chapter discusses the techniques of treatment of long bone metastases.

INTRODUCTION

The role of the orthopedic surgeon in the management of skeletal metastases is to: (1) confirm the diagnosis; (2) treat pathologic fractures; and (3) monitor patients at risk for pathologic fracture. Surgery can play an important role in reducing pain, improving function, and increasing quality of life, even in patients with very short life expectancies. Additionally, aggressive treatment of solitary skeletal metastases may improve long-term survival in selected patients. For example, patients with renal cell cancer and a solitary skeletal metastasis amenable to wide resection can achieve a 30–35% 5-year survival.

All cancer patients with new onset of pain must be assumed to have a skeletal metastasis until proven otherwise. The initial evaluation of such a patient, however, must not rule out the possibility that the lesion is unrelated to the primary cancer. In approximately 45% of cases a solitary hot spot seen on a bone scan in a cancer patient otherwise free of disease is associated with an unrelated process. Needle biopsy has been shown to be effective in diagnosing skeletal

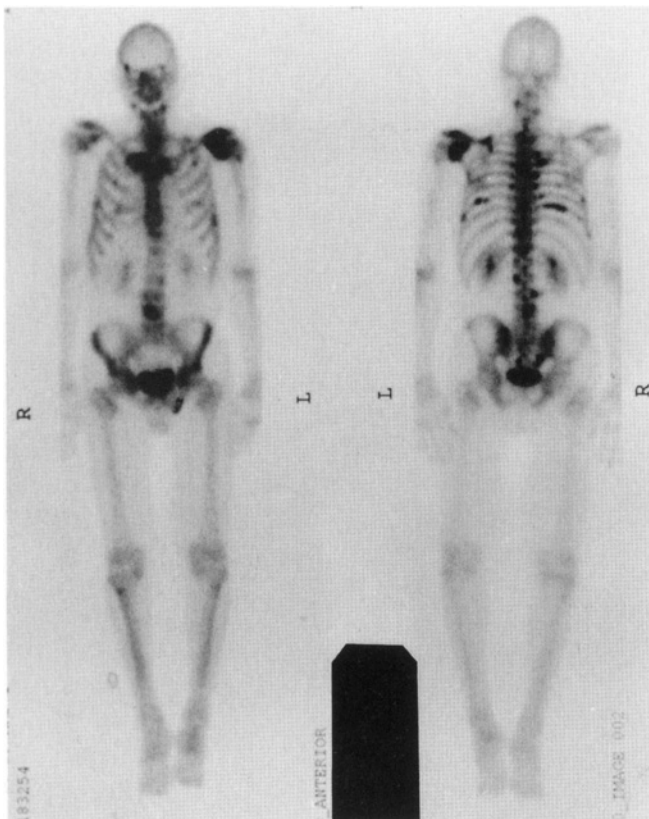


Figure 11.1 Three-phase bone scan showing multiple "hot spots" involving the ribs and shoulder girdle. This demonstrates the typical spread of carcinoma to the skeletal system.

metastases in patients with a history of cancer. Most patients, however, present with multiple skeletal lesions, making the diagnosis of metastatic disease certain.

With few exceptions, patients who present with a painful pathologic fracture are candidates for surgical intervention. Management must be tailored to the individual; this entails balancing the benefit of surgery

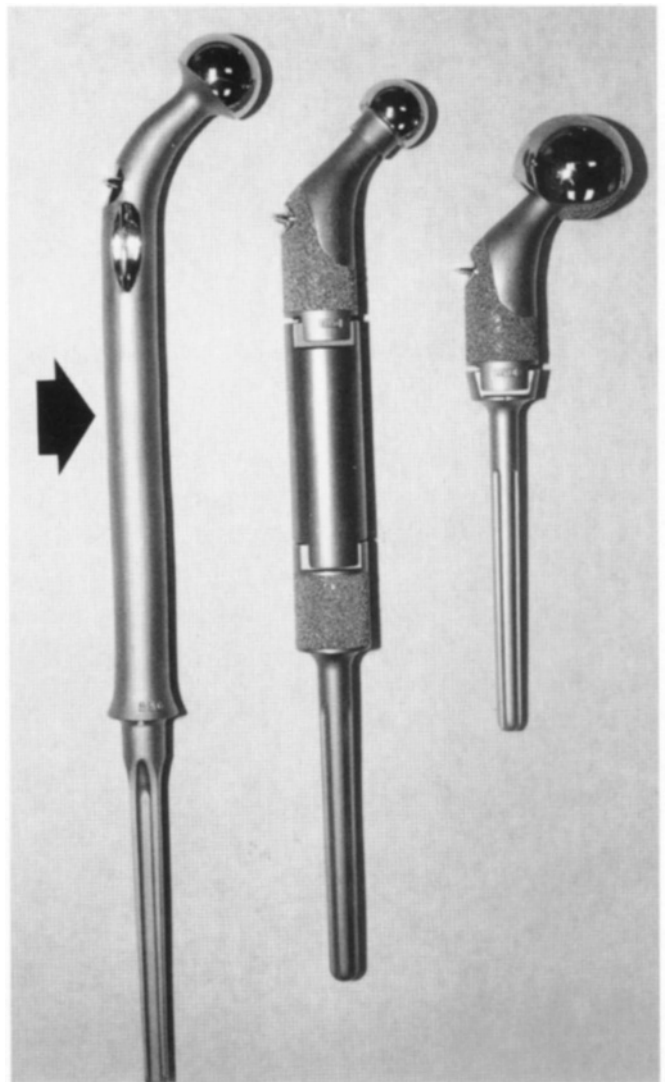


Figure 11.2 Composite photograph showing several types of proximal femoral replacements used to reconstruct large skeletal defects following the resection of metastatic tumors of the proximal femur. The prosthesis (arrow), is a custom prosthesis to replace approximately one-half of the femur. The other two prostheses are modular prostheses that are also utilized in the treatment of primary bony sarcomas. The major indications for segmental replacement of the proximal femur are large, destructive, lytic lesions involving the head, neck, and shaft; solitary metastases; and recurrent tumor following previous attempts at intramedullary fixation with or without cementation.

and the risks associated with operating on a patient with a limited life expectancy and who is in poor medical condition. Isolated fractures of non-weight-bearing bones in the upper extremities can frequently be managed with palliative radiotherapy and casting or bracing. A patient with lower-extremity lesions requires greater use of the upper extremities for transfers and crutch or walker-assisted ambulation. Under these circumstances surgical intervention is often essential. All extremities must be carefully examined before embarking on a course of treatment.

The goals of surgical fixation are to relieve pain, improve function and ambulation, facilitate medical and nursing care, and improve psychological well-being. This requires a different approach from that used for non-neoplastic lesions. Immediate fixation must be obtained at the time of surgery: these patients rarely tolerate multiple surgical procedures. Bony union almost never occurs without surgery and radiotherapeutic treatment. The basic principle of surgical management is internal fixation or prosthetic replacement combined with PMMA. Cementation permits immediate stability and early mobilization and pain reduction.

IMPENDING PATHOLOGIC FRACTURES

Any skeletal lesion may cause a pathologic fracture. Criteria for selecting patients for prophylactic fixation have slowly evolved. Early criteria were based solely on retrospective observations of pathologic fractures in the proximal femur and hip. This was of great importance to orthopedists because of the technological difficulty in fixing such fractures, as well as the high mortality rates associated with hip fractures (Figures 11.3 and 11.4).

The first set of combined guidelines (1986) for prophylactic fixation of proximal femur were:¹ (1) greater than 50% cortical destruction seen on CT, (2) a lytic lesion of the proximal femur > 2.5 cm in diameter, and (3) avulsion of the lesser trochanter. While these guidelines were helpful for lytic lesions of the femur, they failed to account for other patterns of mixed or permeative lesions and would not be readily applied to other sites. In addition, these guidelines failed to account for lesions amenable to nonsurgical treatments. Increasingly, effective adjuvant treatments have resulted in improved patient survival, increasing the time at risk for any given lesion to fracture. Therefore,

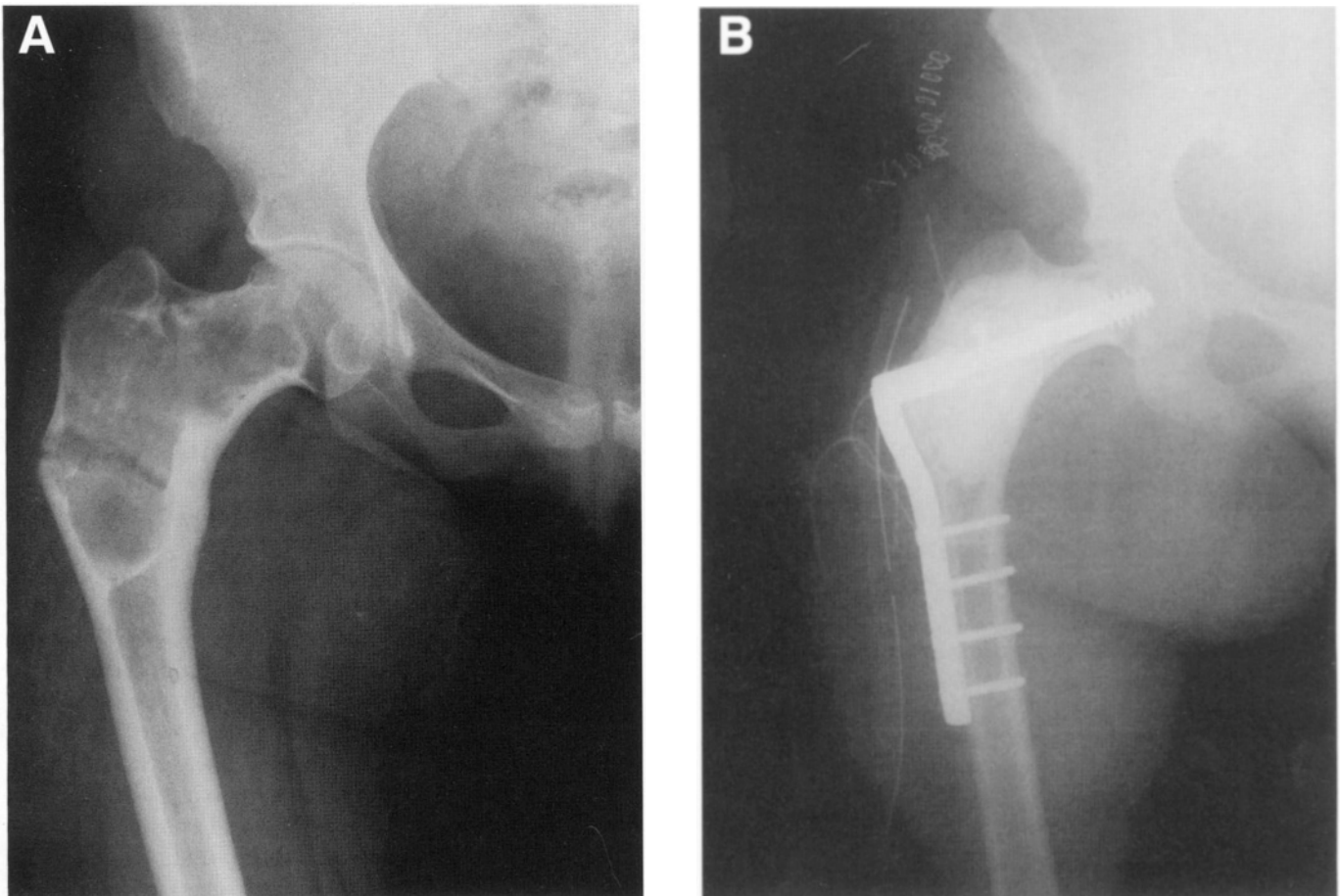


Figure 11.3 (see above and following page).

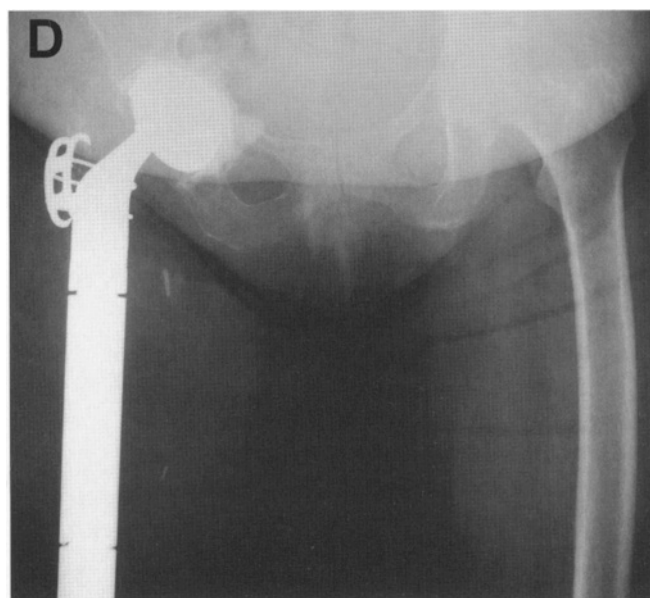


Figure 11.3 (A) Plain radiograph of a pending pathological fracture through a large benign fibrous dysplasia of the proximal femur. (B) Postoperative radiograph following curettage, cementation, and internal fixation. (C) Plain radiograph of the fixation of a multiple myeloma of the lesser trochanteric region of the proximal femur which has progressed despite radiation therapy and fractured with a plate and screws in place. (D) Postoperative radiograph following resection of the proximal femur.

Thompson² revised the Harrington¹ criteria defined as follows: (1) large lytic lesions occupying 50% or more of the cortical diameter unless protected until reconstituted with radiation therapy, medical management, or both; and (2) all destructive lesions of the femoral neck in patients with a survival estimate of > 3 months.

PREOPERATIVE EVALUATION AND INTERVENTIONS

Special preoperative considerations are needed because these patients often have extensive metabolic, hematologic, and nutritional deficiencies. The risk of infection is increased because of possible multiple sources of sepsis (e.g. colostomy, urinary tract infection), neutropenia from chemotherapy or other adjuvant modalities, generalized nutritional deficits, and poor local skin condition from prior radiotherapy or other

procedures. Perioperative antibiotics are recommended for all patients. All patients should have hematologic and clotting evaluation, because many may suffer from anemia of chronic disease or depletion of clotting factors because of a vitamin K deficiency or tumor involvement of the liver. Adequate blood replacement should be available because curettage of many carcinomas – especially myeloma, thyroid tumor, and renal cell carcinoma – often leads to substantial blood loss. The combination of pre-existing anemia and expected blood loss mandates the use of preoperative blood transfusions. Thrombocytopenia occasionally occurs intraoperatively and should be treated aggressively when it occurs. Disseminated intravascular coagulation (DIC) has been noted.

As many of these patients are older, coexisting diseases (e.g. hypertension, diabetes, renal insufficiency, peripheral vascular disease, and cardiopulmonary disease) must be identified and controlled. The presence of other sites of skeletal disease may require special precautions at the time of surgery to prevent additional pathologic fractures. Rib involvement, common in advanced multiple myeloma, may make respiration difficult, leading to prolonged or permanent ventilator dependence following general anesthesia. Specific disorders associated with skeletal metastases

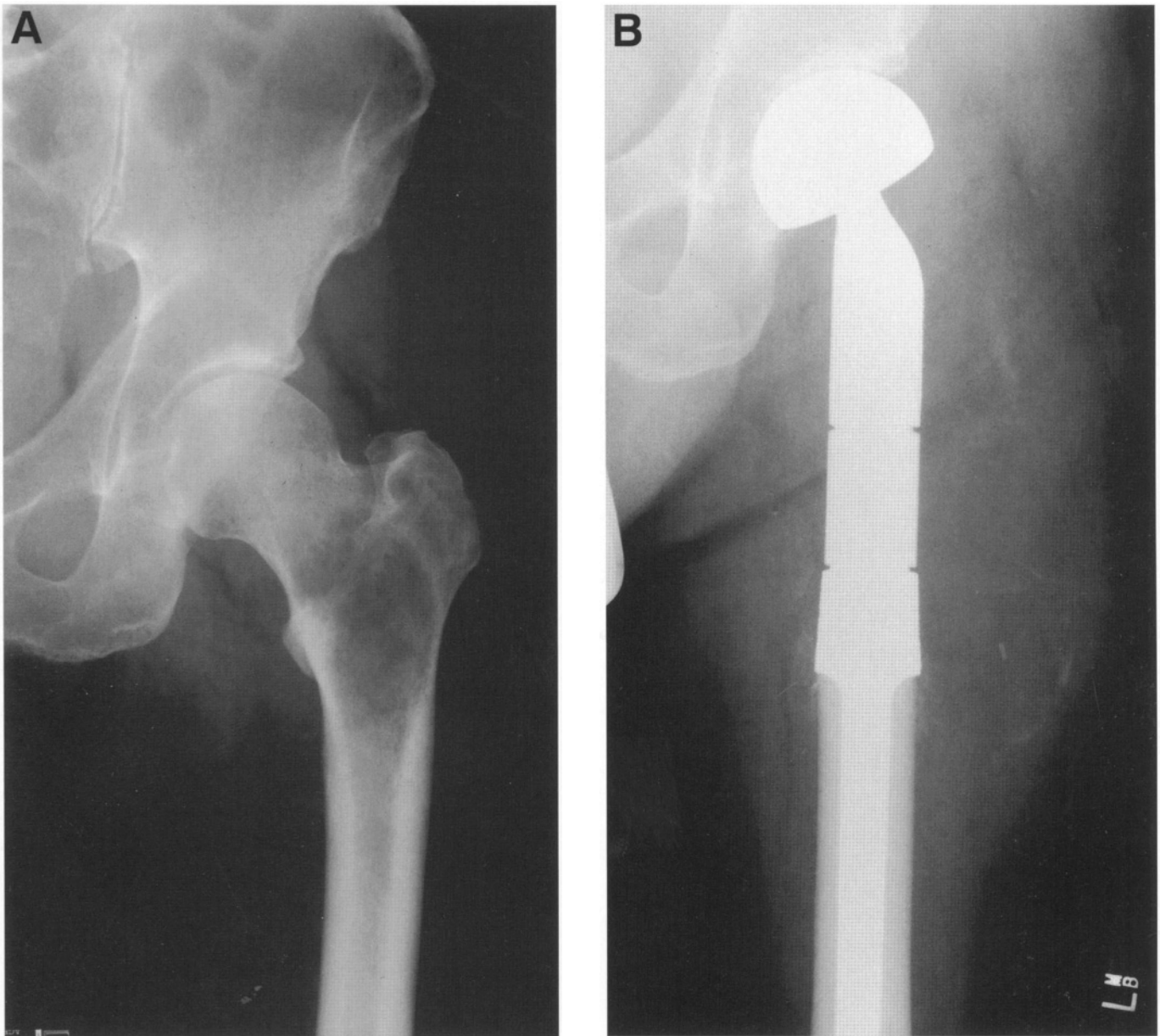


Figure 11.4 Plain radiographs showing a large lytic lesion of the proximal femur secondary to a solitary renal cell carcinoma (A). This patient was treated by a proximal femoral modular segmental replacement (B). It is the choice of the authors to utilize segmental replacements for solitary metastatic tumors, especially renal cell carcinomas, melanomas, and thyroid carcinomas.

must also be controlled. Of particular concern is hypercalcemia, which can lead to sudden death during anesthesia. The use of bisphosphonates, including pamidronate, has been shown to be effective in reducing the serum calcium to normal levels.

Evaluation of the extent of local disease, the amount of bone involved, and the presence of multiple lesions within the same bone are necessary to determine the optimal surgical approach, the amount of tumor to be removed, and the method of reconstruction. The

following are studies commonly used; the choice of imaging techniques depends on the individual patient and tumor location and type.

Bone Scintigraphy

Technetium-99 bone scans can demonstrate the intraosseous extent of tumor and the site of the lesion: whole-body scanning provides information about other possible sites of disease. Additional lesions are

commonly found within the same bone. All lesions within the same bone generally require simultaneous treatment; this usually requires placement of an IM rod or an extended-length endoprosthesis.

Computed Tomography and Magnetic Resonance Imaging

Computed tomography remains the standard for evaluation of cortical bone involvement and is required for lesions of the pelvis, shoulder girdle, and spine. With the exception of lesions being evaluated for prophylactic fixation, it is rarely required for extremity lesions. Tumors of the bony pelvis often have large soft-tissue components that may bleed excessively or lead to mechanical failure of the reconstruction if not recognized preoperatively. MRI is most useful in the evaluation of the soft-tissue extent of the tumor. It can also reveal intramedullary tumor involvement.

Angiography

Diagnostic angiography is not routinely performed; specific indications are pelvic tumors with large extraosseous components and lesions in which preoperative embolization is considered. Patients with metastatic hypernephroma are routinely treated with preoperative embolization because of the potential for extreme, uncontrollable bleeding at the time of surgery (Figure 11.5).

PRINCIPLES OF SURGICAL TREATMENT FOR SKELETAL METASTASIS

Advances in orthopedic techniques and implants have dramatically increased the treatment options for patients with skeletal metastases. Improved metallic alloys, introduction of third-generation interlocked IM rods, advanced prosthetic design, modular segmental replacement endoprostheses, rigid segmental spinal systems, and vertebral body cages permit reconstruction of even the most challenging pathologic fractures. PMMA, used as an adjunct to fixation devices (intramedullary rods,

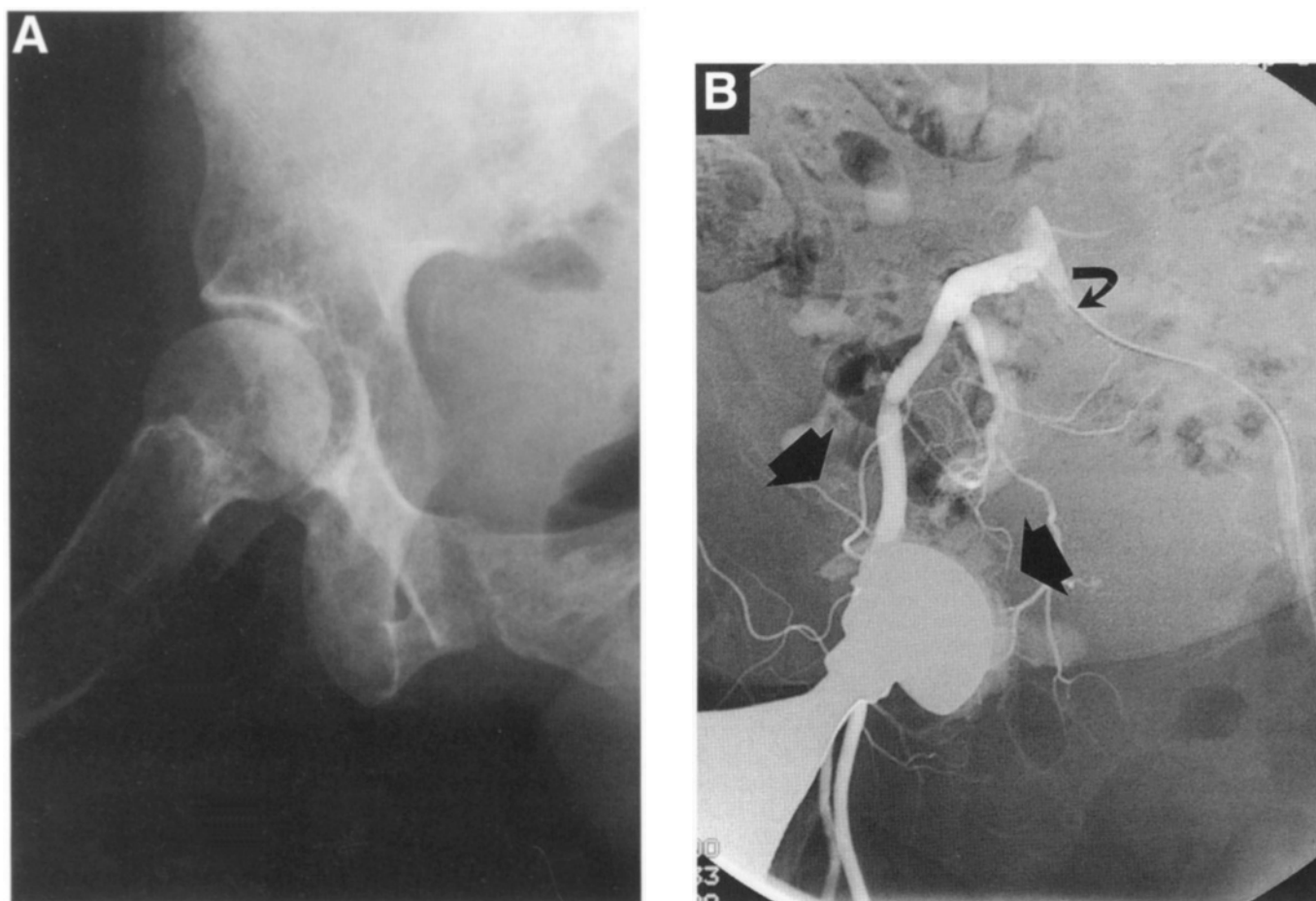


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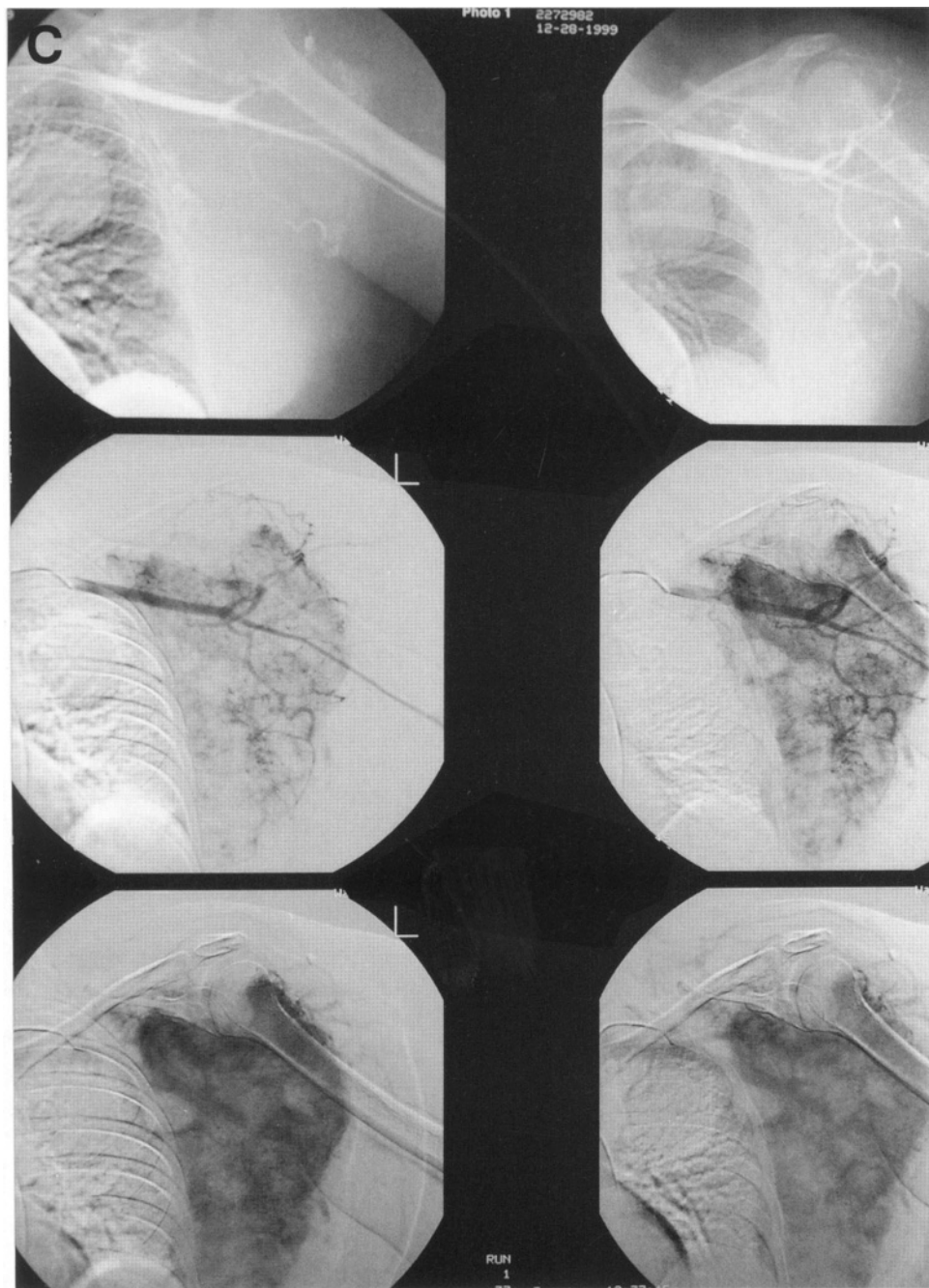


Figure 11.5 (see above and following page).

plates and screws) and prostheses permits instant reconstruction of large defects and immediate stabilization. Adjuvant treatment of the tumor is necessary to protect the reconstruction. Therefore, all patients with skeletal metastases require a multidisciplinary approach coordinating chemotherapy and radiation with surgical intervention.

Principles of management of pathologic or impending fractures are as follows:

1. Preoperative embolization of suspected vascular tumors.
2. Administration of perioperative antibiotics.
3. Correction of underlying hypercalcemia.
4. Transfusion to correct pre-existing anemia, thrombocytopenia and coagulation deficits.
5. Modification of standard surgical approaches to avoid prior radiation fields and ensure adequate soft-tissue coverage and closure.



Figure 11.5 Angiography with embolization of a large metastatic thyroid carcinoma to the right periacetabulum. The superacetabular region is a common area for metastatic disease from renal cell and thyroid carcinomas. (A) Plain radiograph prior to embolization. (B) Angiography following embolization showing absence of vascular blush within the superacetabular region. Note: this patient had undergone a prosthetic replacement of the hip for a stress fracture through irradiated bone unrelated to the carcinoma. The curved arrow indicates the obliteration of the hypogastric (internal iliac) artery which has been embolized prior to surgery. Solid arrows show the periacetabular area with complete absence of tumor vascularity. (C) Angiography of a large renal cell carcinoma replacing the entire scapula; time sequence injection study. (D) Post-embolization showing almost a complete absence of vascularity. This patient was treated by a total proximal humerus and scapula resection (Type IV).

6. Curettage to remove all gross disease.
7. Use of immediate rigid fixation consisting of internal fixation with PMMA or cemented prosthetic replacement.
8. Filling of defects with PMMA.
9. Postoperative nutritional supplementation to promote wound healing.

10. Adjuvant radiotherapy, with or without adjuvant chemotherapy.

The common local surgical procedures for metastatic tumors of the extremities are: tumor excision, composite osteosynthesis, joint replacement, segmental reconstruction, cryosurgery and amputation.

Tumor Excision

Tumor removal and bone stabilization best meet the goals of diagnosis, functional stability, and pain relief. For this reason the metastatic lesion should generally be curetted. Treatment options include intralesional (marginal) and extralesional (wide) excision. Intralesional curettage of tumor is usually performed in or around a fracture site at the time of stabilization (Figure 11.6). Extralesional excision, i.e. resection, is usually performed for a solitary metastatic lesion.

Composite Osteosynthesis

Internal fixation devices (bone plates, screws, IM rods and nails) are used to stabilize impending or actual pathologic fractures. This technique is most often used for metastatic lesions in the diaphysis of long bones, most commonly the humerus and femur.

Joint Replacement

Joint replacement entails resection and reconstruction of a joint using a prosthesis combined with PMMA. Hemijoint replacement involves resection of half of the joint surface and adjacent bone. Total joint replacement is rarely required. Metastatic lesions of the proximal femur are most commonly treated by endoprosthetic replacement.

Segmental Reconstruction

Segmental reconstruction is the resection of a large segment of bone combined with segmental prosthetic replacement and PMMA. This technique is less common than joint replacement and is used for large lesions for which the remaining bone cannot be reconstructed by cementation and internal fixation (Figures 11.7 and 11.8).

Cryosurgery

Cryosurgery is the use of liquid nitrogen as a surgical adjunct to tumor curettage to freeze any residual tumor cells. It may be combined with any of the above procedures in order to increase local tumor control.

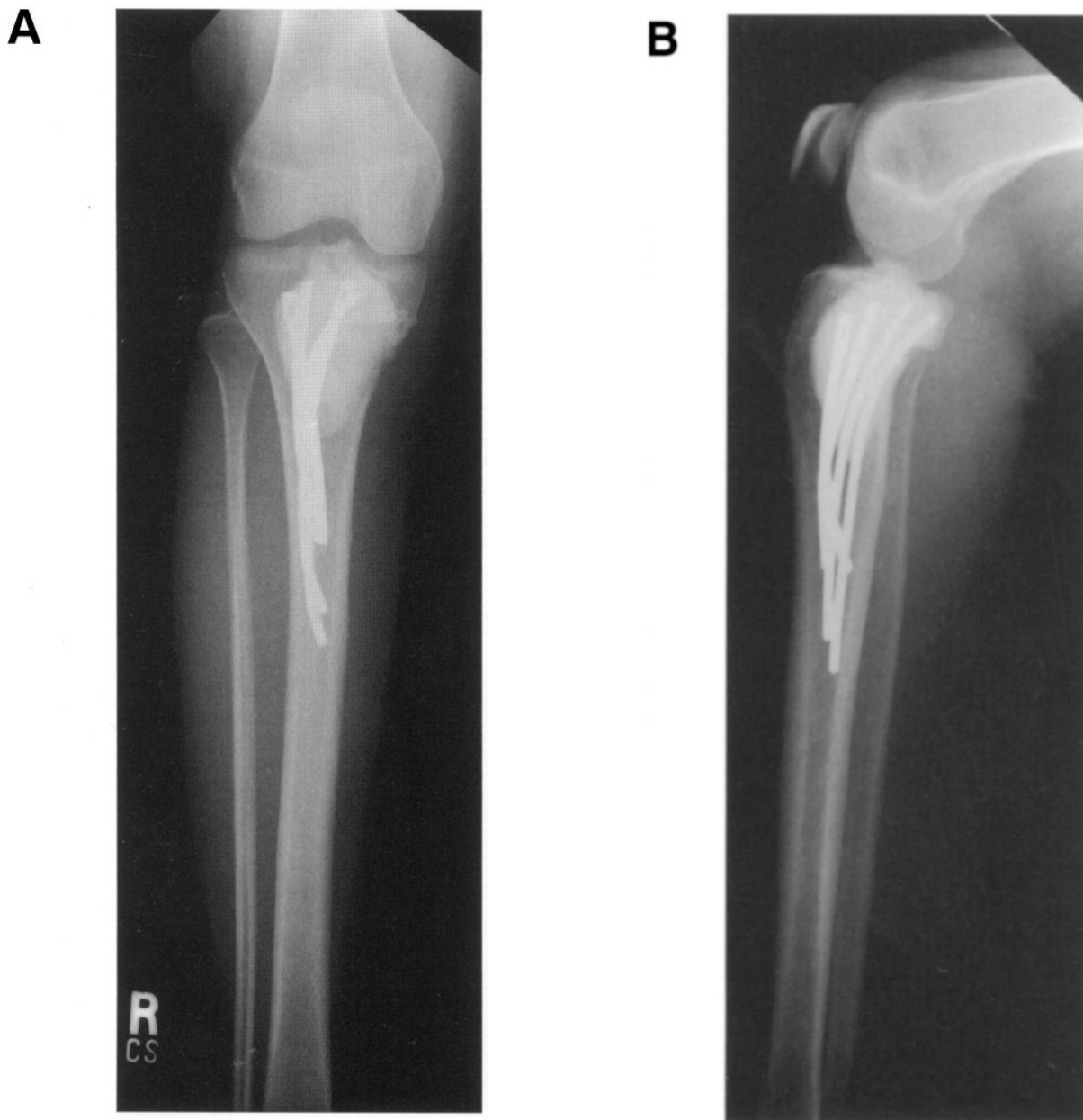


Figure 11.6 Anterior–posterior (A) and lateral (B) plain radiographs following curettage, cryosurgery, cementation, and internal fixation of a large lytic lesion of the proximal tibia for a metastatic melanoma. Cryosurgery was utilized in an attempt to gain local control in addition to postoperative radiation therapy.

Amputation

Amputation has a limited, but definite, role in the management of metastatic cancer. It is occasionally indicated only when advanced cancer results in uncontrollable or intractable pain, a functionless extremity, tumor fungation, sepsis, or erosion and hemorrhage of a major vessel at the tumor site. These complications occasionally occur after inadequate local tumor control. The goal of amputation is to eliminate pain or sepsis and restore function.

Forequarter amputation may be required for recurrent breast carcinoma involving the brachial plexus and axillary vessels.

SPECIFIC ANATOMIC SITES

Pelvis and Acetabulum

Lesions of the hemipelvis not directly involving the hip joint can generally be treated with modification of weight-bearing and external beam radiation. Avulsion

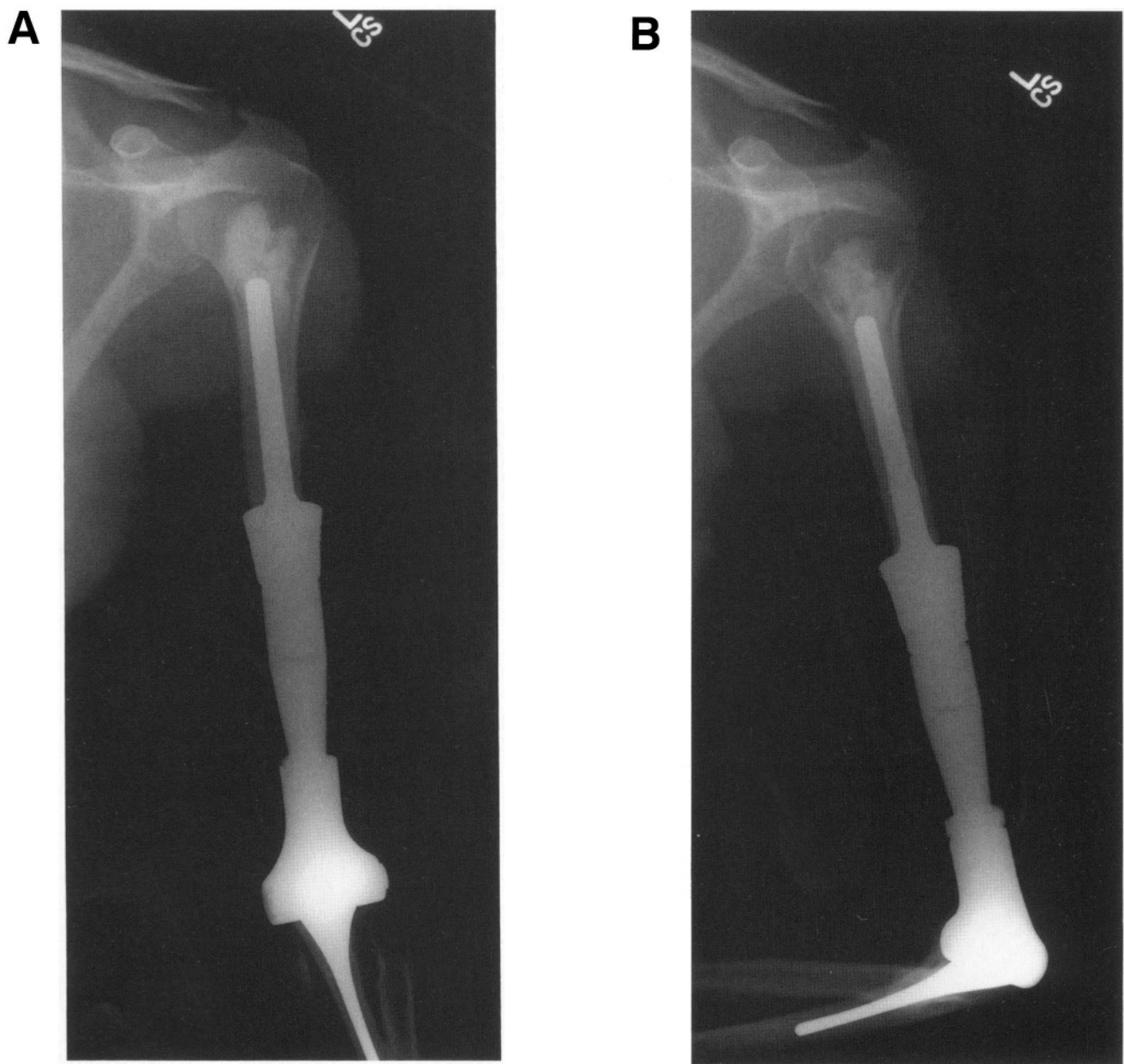


Figure 11.7 Anterior–posterior and lateral photographs of a large segmental replacement of the distal humerus and elbow joint for a large destructive melanoma of the elbow. (A) shows the AP view; (B) shows the lateral view. Melanomas, similar to renal cell carcinomas, may cause large lytic destruction of a bone simulating a primary sarcoma. Local control is often difficult to obtain. The authors prefer resection of large metastatic melanomas.

fractures of the anterior superior/inferior iliac spines, iliac crest, and superior/inferior pubic rami are common and should be treated nonoperatively. Large supra-acetabular lesions that do not respond to radiotherapy should be curetted and packed with PMMA combined with Steinmann pin fixation (Figures 11.9 and 11.10).

Proximal Femur (Hip)

The hip is the most common site of pathologic fracture. This is because of the high incidence of metastases in this area and the magnitude of force concentrated in this area with normal activity. In general, all pathologic

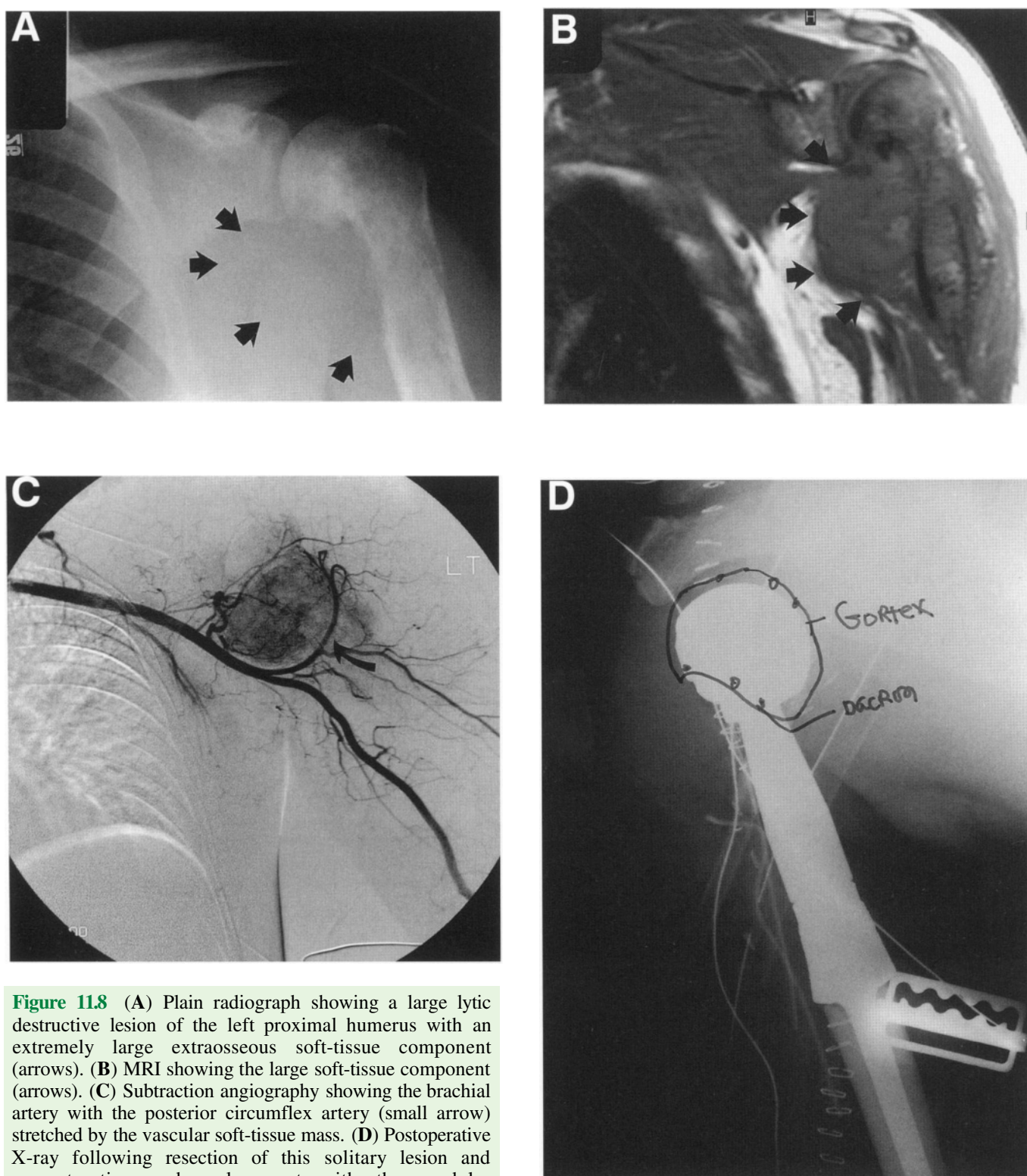


Figure 11.8 (A) Plain radiograph showing a large lytic destructive lesion of the left proximal humerus with an extremely large extraosseous soft-tissue component (arrows). (B) MRI showing the large soft-tissue component (arrows). (C) Subtraction angiography showing the brachial artery with the posterior circumflex artery (small arrow) stretched by the vascular soft-tissue mass. (D) Postoperative X-ray following resection of this solitary lesion and reconstruction and replacement with the modular segmental replacement prosthesis. Note: Gore-Tex[®] graft is utilized to stabilize the humeral head, neck, and glenoid joint. The Gore-Tex[®] is reinforced by Dacron tape as noted. Large solitary metastatic tumors to the skeletal system with large extraosseous components are best treated by primary resection.

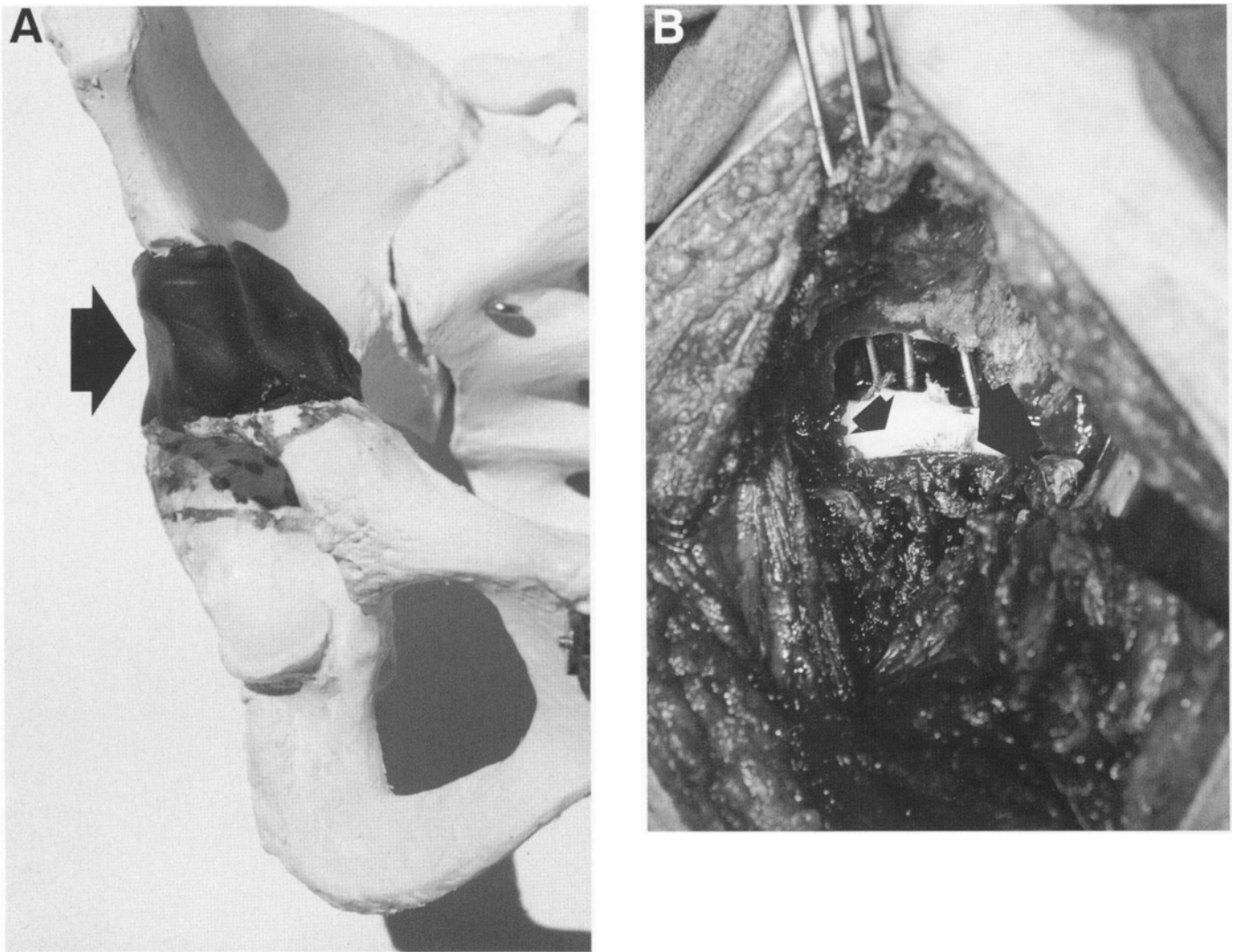


Figure 11.9 (A) A plastic model of the pelvis with a large superacetabular tumor demarcated by the dark area (arrow). The superacetabular area of the ilium is a common area of metastases for many types of carcinomas, especially metastatic renal cell carcinoma and thyroid carcinoma. (B) Intraoperative photograph showing a curetted defect corresponding to the lesions seen in (A) and reconstructed with a polyethylene spacer (large arrows) held in place by Steinmann pins. This defect is then reinforced with methylmethacrylate. This procedure was developed by the senior author and is used to avoid the more complicated and increased morbidity associated with a total hip replacement. The technique of curettage and polyethylene replacement is extremely safe and reliable.

fractures of the hip require surgical reconstruction and postoperative radiation. Surgery is often warranted even in the severely weakened, nonambulatory patient; to relieve pain, to simplify nursing care, and to regain transfer ability.

Radiographs and bone scans of the femur and acetabulum must be obtained preoperatively. It is not uncommon to detect other lesions further down the shaft; a situation that indicates the need for simultaneous fixation. In general, a long-stem prosthesis will be adequate for both femoral neck and diaphyseal

lesions. If the acetabulum is affected by disease, surgery should include curettage of the lesion (Figure 11.11).

Surgical Treatment

Metastatic fractures of the hip may be intracapsular (involving the femoral neck), intertrochanteric, or subtrochanteric. Surgical treatment of intracapsular fractures entails endoprosthetic replacement (usually long-stem) or total hip replacement (Figure 11.12). Management of intertrochanteric and subtrochanteric fractures varies;

plate and screw fixation (with PMMA) and second-generation femoral rods (with fixation extending across the femoral neck), respectively, have been described. We recommend long-stem prostheses with PMMA for metastatic involvement of any area of the hip. This is reliable and simple, avoids late failure of fixation, simultaneously treats lesions more distal in the shaft, and permits early mobilization.

Technique

A standard posterolateral approach is most often utilized. The trochanter should not be osteotomized. The head and neck are removed and the canal is reamed with *flexible* reamers (solid reamers may perforate the abnormally thin bone). The stem of the prosthesis should extend at least to the isthmus or be distal to any shaft lesions. The incision may be extended to allow resection or curettage of all gross tumor. Absent bone can be reconstructed with PMMA.

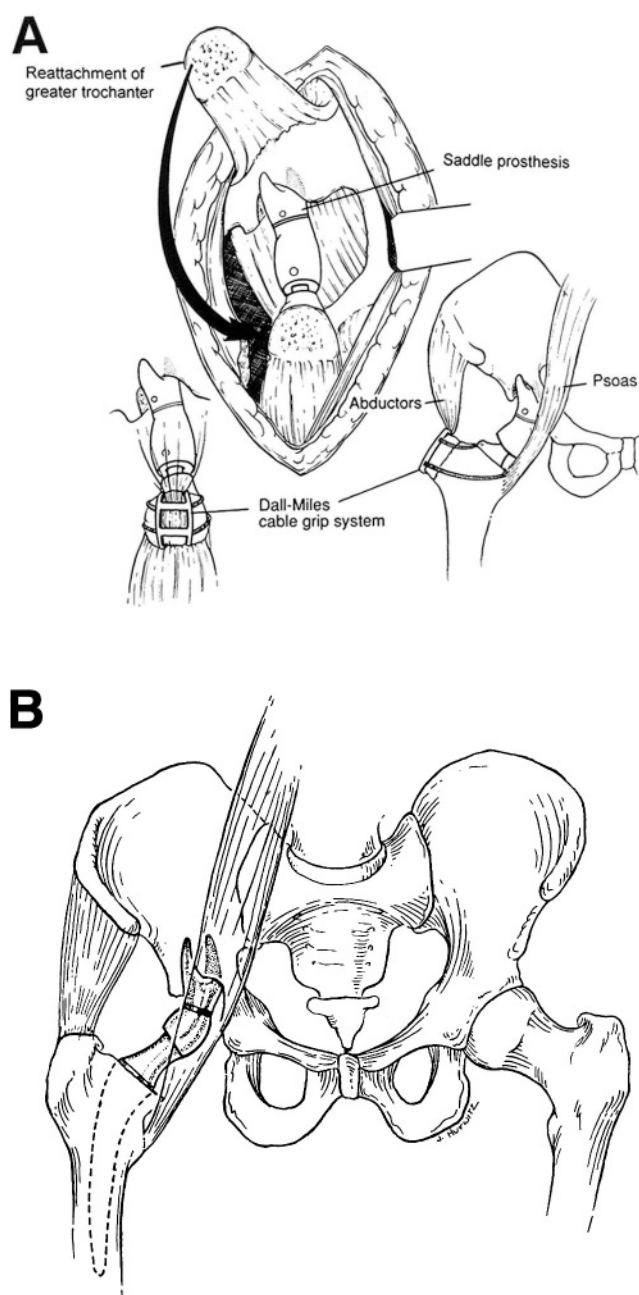


Figure 11.10 (see above and following page). Seminars in Arthroplasty, Vol. 10, No. 3 (July) 1999

It is extremely important to obtain a good cement mantle around the stem of the prosthesis and distal to the prosthetic tip. The PMMA should be cooled before injection to increase the time of polymerization. If loss of proximal bone loss is extensive, a segmental prosthesis is utilized. This technique can successfully reconstruct large proximal defects; however, it is associated with

significant operative morbidity and not routinely performed. Postoperatively the patient is mobilized within 2–3 days; full weight-bearing on the involved extremity.

Femoral Shaft

Generally, the most appropriate means of stabilizing impending or actual pathologic fractures of the femoral shaft is second-generation IM nails with locking capabilities proximally and distally. Combined osteosynthesis (i.e. plate-and-screw fixation and PMMA) may be successful; however, it is not preferred because of the risk of fracture proximal and distal to the plate, increased operative time, and the need for more extensive surgical exposure. IM rod fixation is generally done by the "open" method, i.e. the tumor/fracture site is exposed, the tumor is curetted, PMMA is injected proximal and distal, and the IM rod is inserted. The proximal and distal fragments are reamed of all gross disease to permit easy insertion of the PMMA and rod. A uniform cement mantle should be obtained around the rod. The need to open and visualize the tumor and augment it with PMMA is dependent on the size and



Figure 11.10 (A) Schematic technique for saddle reconstruction of large defects of the acetabulum. The lateral approach is utilized and a trochanteric osteotomy is performed. The acetabulum is curetted and removed and is reconstructed with a femoral component with a specially designed saddle prosthesis manufactured by Link America[®]. The trochanter is then reattached with cables. It is important to note that the stability of this reconstruction is dependent on the abductor and psoas muscles being present and placed under the correct tension by the correct length of the body segment of the saddle prosthesis. (B) Schematic diagram of reconstruction following resection of a periacetabular tumor with a saddle prosthesis. *Note:* the saddle component is not fixed to the ilium but is placed in a notch such that the two horns of the saddle lie internal and external to the ilium. The femoral component is cemented into the femoral canal. This provides immediate fixation and stability equivalent to the standard total hip replacement. The major advantage of this technique is that surgical morbidity is markedly decreased when compared with a standard total hip replacement combined with a difficult reconstruction of the acetabulum which requires an oversized cup, Steinman pins and PMMA. (C) Saddle prosthesis (Waldemar-Link, Hamburg, Germany). This prosthesis consists of three components: femoral stem, base element (body), and the saddle component. The saddle sits in a notch made by the surgeon in the remaining ilium. The base elements are available in variable lengths. (D) Plain pelvic radiograph showing a large, lytic, destructive, supra-acetabular lesion (arrows) from a long-standing myeloma. This patient was non-ambulatory for 6 months. (E) Postoperative photograph 1 year following resection of the tumor and reconstruction with a saddle prosthesis.

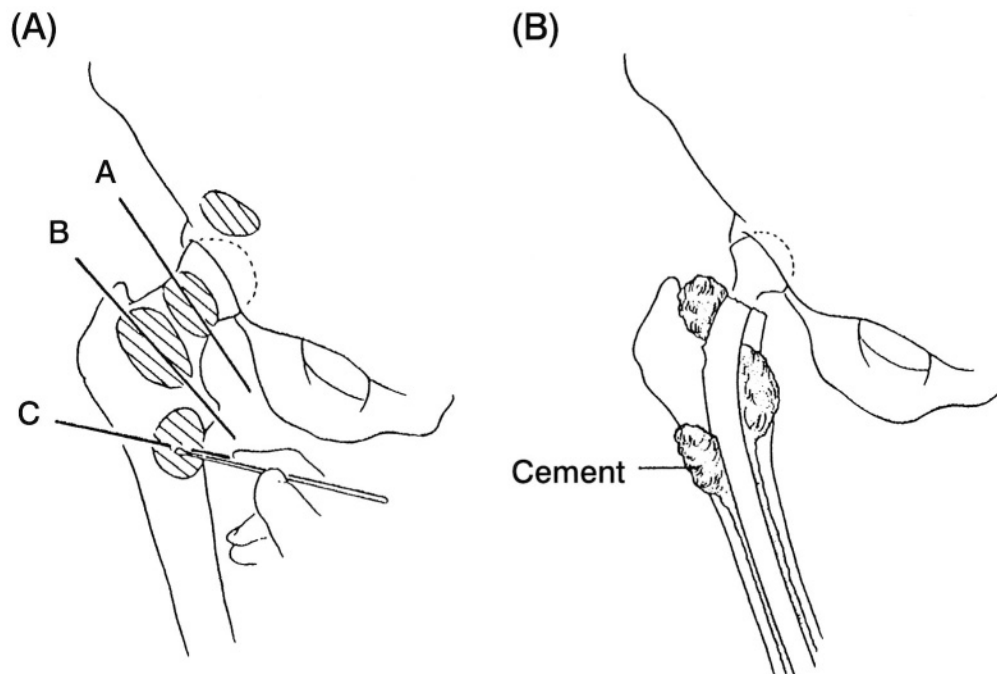


Figure 11.11 (A) Schematic diagram of common sites of metastases of the hip. (B) Technique of curettage and cementation of the tumor defect combined with a long stem endoprosthesis (bipolar type). Fixation for metastatic tumors of the hip is one of the most common sites of pathological fracture.

degree of cortical destruction. Immediate ambulation with full weight-bearing is permitted within a few days after surgery. Pain relief is almost universal and approximately 90% of patients maintain ambulation.

Prophylactic Femoral Shaft Fixation

Small lesions of the femoral shaft may be treated prior to fracture by the "closed" method; that is, fluoroscopically inserting an IM rod from a small incision at the tip of the greater trochanter and antegrading it through the lesion to obtain good distal fixation. When utilizing this procedure it is difficult to insert PMMA, and this method is therefore indicated only for small lesions of the femoral shaft with normal proximal bone. Careful preoperative evaluation of the hip is required, because subsequent treatment of an undetected hip lesion is extremely difficult once an IM rod is in place.

Supracondylar Femoral Fixation

Metastatic lesions of the distal femoral diaphysis and condyles are best treated by medial and lateral Zickel rods with PMMA. Large distal femoral metaphyseal lesions, especially those associated with intra-articular extension and/or large soft-tissue components, are best

treated with a custom or modular distal femoral endoprosthetic replacement.

Humerus

Surgical stabilization is recommended for patients at risk for fracture and in whom stable fixation can be assured. It is also recommended to permit crutch/walker use in patients with concomitant lower extremity lesions. Large lesions, or those with a pathologic fracture, are best treated by curettage, intramedullary fixation, and PMMA. Treatment options for the proximal humerus (metaphysis, surgical neck and head) include stabilization with plate and screws or IM rods supplemented with PMMA and conventional or custom head and long-stem endoprosthetic replacement. Proximal humeral lesions are approached through a standard deltopectoral incision. Tumors of the shaft may be treated with antegrade or retrograde intramedullary nailing, plate-and-screw fixation augmented with PMMA, and customized diaphyseal spacers.

Lesions of the distal humerus are a difficult therapeutic challenge. Treatment options include crossed rush rods introduced into medial and lateral epicondyles, medial and lateral column reconstruction with plate-and-screw constructs supplemented with

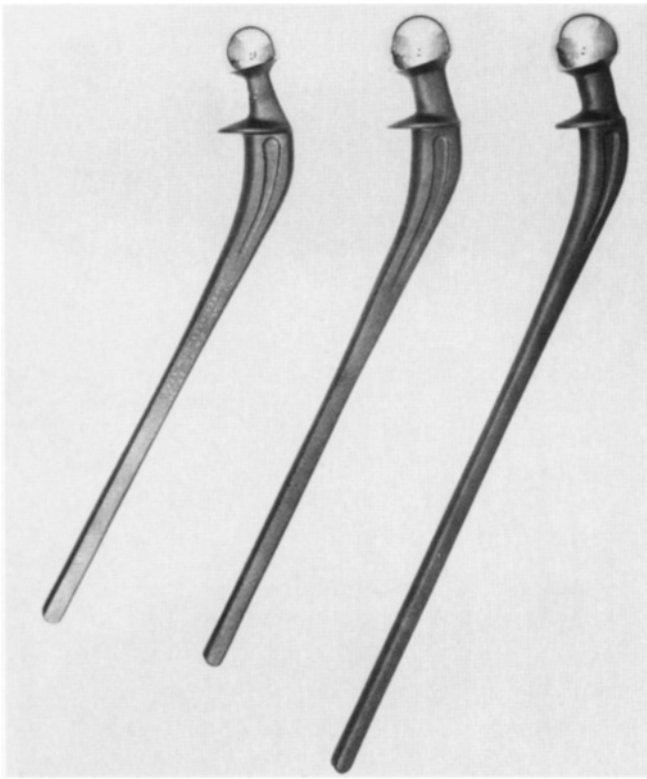


Figure 11.12 Composite photograph of various sizes of long stem femoral prostheses.

PMMA, and conversion to a long-stem (humeral and ulnar) constrained elbow arthroplasty. The surgical exposure should not include olecranon osteotomy because of the likelihood of nonunion with postoperative radiotherapy.

Lesions Distal to the Knee and Elbow

The most common primary cancers associated with distal metastases are those of the lung, kidney, breast, and gastrointestinal tract. Tumors of the forearm or tibia are best treated by IM fixation with supplemental PMMA. Tumors of the hand often require amputation because of extensive bony destruction. Substantial experience with extremity preservation has been accumulated with multimodality therapy for primary sarcomas of the hand and foot; however, this experience often does not apply to the management of metastases at these sites. Radiation should be used for attempted palliation in patients with metastatic disease to the hand or foot. Amputation may be used for patients who do not respond to radiotherapy.

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Section 2

Muscle Group Resections

Buttockectomy

Martin Malawer and Paul Sugarbaker

OVERVIEW

Tumors of the gluteus maximus (buttock) are often extremely large before diagnosis. Traditionally, low- and high-grade soft-tissue sarcomas of the buttock were treated by a posterior cutaneous flap hemipelvectomy. Today, however, most low-grade soft-tissue sarcomas of this muscle can be resected with safe margins. Hemipelvectomy is not required. Resection involves complete removal of the gluteus maximus muscle and ligation of the inferior gluteal vessels. The underlying sciatic nerve is preserved. Most high-grade sarcomas of the gluteus maximus can similarly be treated by surgical resection. Preoperative induction chemotherapy, intra-arterial chemotherapy, or radiation therapy is required. Radiation therapy may also be required depending on final margins.

The gluteus maximus is a "quiet area" for soft-tissue sarcomas. The only significant structure that must be evaluated is the sciatic nerve. Minimal reconstruction is required. During the postoperative period it is important to take measures to prevent the formation of large postoperative seromas. The functional outcome of a resection of the gluteus maximus is a minimal deficit in hip extension only. The gait is normal.

Today a hemipelvectomy is rarely required for most soft-tissue sarcomas unless they are extremely large and/or are accompanied by fungation, infection, or extension into the ischiorectal space, pelvis, and hip. Direct sacral involvement, which is rare, necessitates an amputation.

INTRODUCTION

The gluteus maximus is a common site for high- and low-grade soft-tissue sarcomas. Such lesions are often confined to the gluteus maximus and do not extend to the underlying retrogluteal space or involve the sacrum or femur. Therefore, a majority of them have traditionally been treated by a wide local resection. Extremely large tumors of the gluteus maximus were, by contrast, traditionally treated by a posterior cutaneous flap hemipelvectomy. An anterior myocutaneous flap modification has been devised by Sugarbaker *et al.*¹ The development of limb-sparing procedures has reduced the need for hemipelvectomy for tumors in this region. Today approximately 90% of soft-tissue sarcomas arising in the buttocks can be resected and adequately treated by a limb-sparing resection. Low-grade soft-tissue sarcomas of the gluteus maximus require surgery only; high-grade soft-tissue sarcomas in this region, like those in other anatomic areas, are treated by either induction chemotherapy and/or radiation therapy preoperatively followed by postoperative chemotherapy. We favor the use of induction chemotherapy followed by a limb-sparing resection when possible. The field is treated with postoperative radiation if required. The major indications for an amputation are extremely large sarcomas that involve the adjacent bone, sciatic nerve, or the ischiorectal fossa.

UNIQUE ANATOMIC CONSIDERATIONS

The gluteus maximus arises from the sacral lamina and alar iliac crest and obliquely passes to its insertion onto the proximal portion of the iliotibial band. This insertion begins above the greater trochanter, passes 4–5 cm below the greater trochanter, and then attaches to the adjacent femur. The gluteus maximus does not attach to the retrogluteal structures as it passes over them. This permits easier surgical dissection of the retrogluteal plane and preservation of the sciatic nerve in many situations.

As it passes from the sacrum to the femur the gluteus maximus covers the sacroiliac joint and the sacrospinous and sacrotubulous ligaments, as well as a portion of the ischiorectal fossa. The area deep to the gluteus maximus is termed the "retrogluteal space". This area consists of the posterior hip musculature, including the external rotators and portions of the gluteus medius muscle. Most important, the sciatic nerve exits the pelvis through the sciatic notch and passes inferiorly to the piriformis muscle. This nerve lies in close proximity to the posterior fascia of the gluteus maximus; therefore, large tumors of the gluteus maximus may involve the sciatic nerve. The sciatic nerve is rarely involved by the tumor; most often it is displaced around the capsule or

pseudocapsule. The inferior vessels pass below the piriformis muscle to enter the midportion of the gluteus maximus. The inferior gluteal vessels are routinely ligated.

INDICATIONS

A gluteus maximus resection is indicated for patients with low- and high-grade sarcomas confined to the gluteus maximus.

CONTRAINDICATIONS

Possible contraindications to gluteus maximus resection include the following:

1. Large tumors that involve the true pelvis or ischiorectal space.
2. Involvement of the sacrum or ilium.
3. Sciatic nerve involvement (although, on occasion, the sciatic nerve may be resected).
4. Pelvic extension through the sciatic notch.

IMAGING STUDIES

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

These studies are most useful in determining the extent of tumor involvement of the gluteus maximus (Figures 12.1–12.3). Close evaluation will determine the involvement of the adjacent sacrum, femur, and sciatic nerve. Attention should be placed on the evaluation of the structures of the retrogluteal space, including the hip joint and sciatic nerve, and ischiorectal fossa. Buttock tumors may extend into the pelvis through the sciatic notch.

Bone Scan

Tumor involvement may extend to the crest of the ilium, the sacrum, and the proximal femur. These areas should be evaluated by bone scintigraphy.

Angiography

Angiography is not routinely performed when evaluating tumors of the gluteus maximus (Figure 12.1D). It may be useful in preoperative embolization or preoperative intra-arterial chemotherapy.

Biopsy

The biopsy site must be in line with the incision for the hemipelvectomy should one be required (Figure

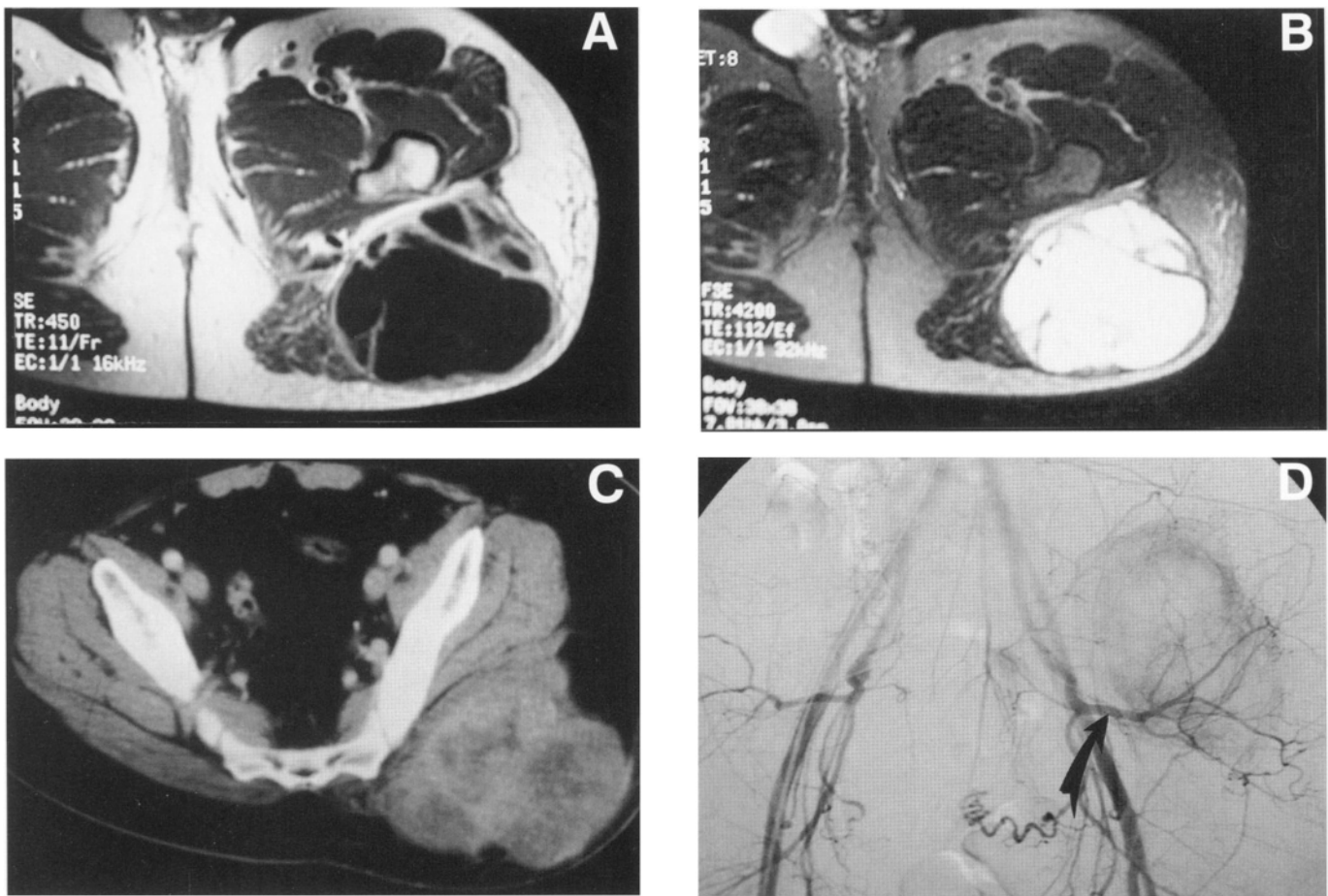


Figure 12.1 Radiographic evaluation of a patient with a large buttock sarcoma. (A, B) T1 and T2 weighted MRI images of a large buttock sarcoma. Note that on the T1 the lesion is extremely large, involving the entire gluteus maximus but without extension into the pelvis or into the anterolateral aspects of the thigh. The T2 weighted image shows a blood-filled cavity that is the result of a spontaneous bleed into the tumor following induction chemotherapy. (C) CT scan of a large buttock sarcoma involving the entire gluteus maximus but not involving the abductor muscles or showing any evidence of intrapelvic extension. (D) Late-phase angiography showing a typical tumor blush of the left buttock tumor. This represents extremely viable tumor despite induction chemotherapy. This patient was still a good candidate for a limb-sparing procedure. Note (arrow) the main vascular supply is from the gluteal vessels that supply the buttock area. These vessels are exposed and ligated early in the operative procedure.

12.4A). Surgeons performing a biopsy of tumors of the buttock must therefore be familiar with the surgical incisions for both posterior flap hemipelvectomy and anterior flap hemipelvectomy. The anterior flap hemipelvectomy, as described by Sugarbaker *et al.*, is preferred for large sarcomas of the buttock area. In this procedure the entire musculature and skin is removed with the amputation and the anterior myocutaneous flap consisting of the quadriceps muscle is utilized to close the defect. If a posterior flap is utilized, care must be taken not to contaminate the posterior skin or fascia. The biopsy site must therefore be along the lateral aspects of a posterior incision and must avoid the greater trochanter, sciatic nerve, ischiorectal fossa, and greater trochanter.

SURGICAL GUIDELINES

1. A large curvilinear incision is made beginning at the posterior aspect of the crest of the ilium, curving distally following the gluteus maximus muscle along the iliotibial band (Figure 12.5), passing over the greater trochanter to about 6 cm distal, and then curving posteriorly back toward the inner aspect of the thigh along the gluteal fold. This incision makes it possible to elevate a large posterior flap.
2. To determine resectability or operability, the sciatic nerve is identified distal to the resection site. This can be identified between the medial and lateral hamstring muscles or just lateral to the ischium before it passes underneath the gluteus maximus muscle.

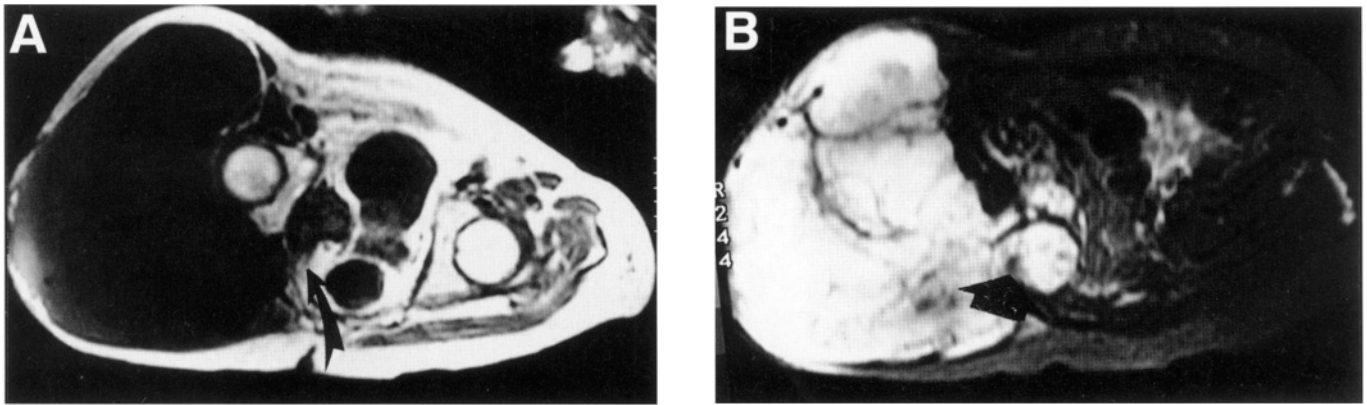


Figure 12.2 MRI scans of a patient with a large buttock sarcoma considered unresectable that required a hemipelvectomy due to intrapelvic extension of the tumor. (A) T1 weighted image of a MRI scan showing a huge right buttock sarcoma involving the entire gluteus maximus and extending into the anterior thigh compartment. In addition, there is obvious extension into the pelvis through the sciatic notch (arrow). This is the most important area to evaluate for pelvic extension and is the most common route of intrapelvic disease. (B) T2 weighted MRI image of (A) showing obvious involvement of the acetabulum as well as the intrapelvic extension. This patient underwent an extended anterior flap hemipelvectomy due to extension into the pelvis as well as the sacrum (seen on other views).

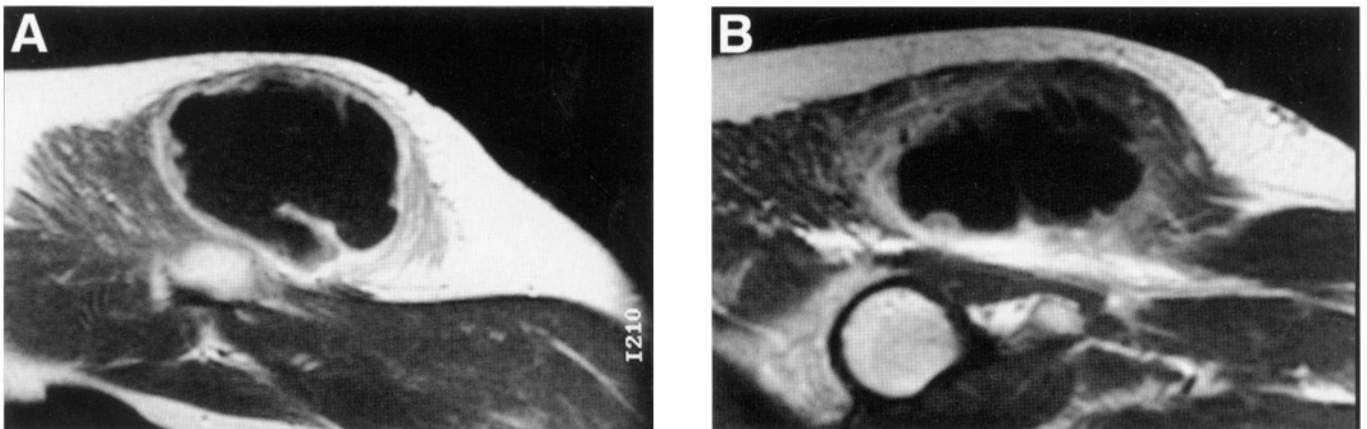


Figure 12.3 (A and B) Coronal MRI views. T1 weighted image of a large buttock sarcoma. Note there is no extension distally or to the adjacent hip joint.

The nerve is palpated below the gluteus maximus muscle toward the piriformis muscle.

3. The gluteus maximus is detached from the iliotibial band throughout its length and from the femur distally. This muscle is then flapped medially to expose the superior and inferior gluteal vessels that are then ligated. The sciatic nerve is displaced anteriorly to protect it during the dissection.
4. Removal of the gluteus maximus involves detaching this muscle from the sacrotuberous and sacrospinous

ligaments, as well as the lamina and sacral alar.

5. To prevent a large postoperative seroma, great care must be taken to tack down the large posterior fasciocutaneous flap to the remaining underlying muscle. Multiple, large drains are utilized.
6. The patient remains supine for 72 h to prevent the development of a seroma.

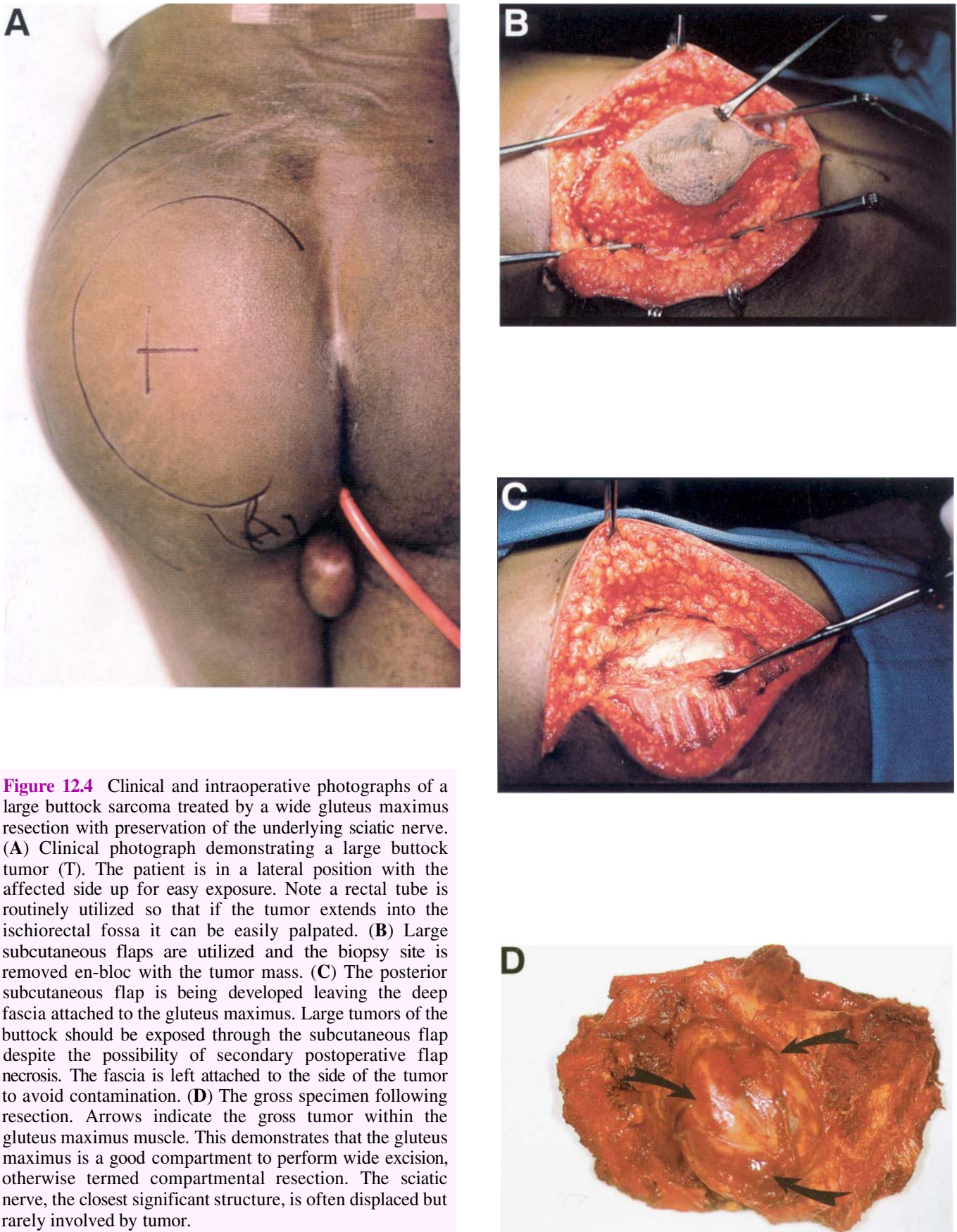


Figure 12.4 Clinical and intraoperative photographs of a large buttock sarcoma treated by a wide gluteus maximus resection with preservation of the underlying sciatic nerve. (A) Clinical photograph demonstrating a large buttock tumor (T). The patient is in a lateral position with the affected side up for easy exposure. Note a rectal tube is routinely utilized so that if the tumor extends into the ischiorectal fossa it can be easily palpated. (B) Large subcutaneous flaps are utilized and the biopsy site is removed en-bloc with the tumor mass. (C) The posterior subcutaneous flap is being developed leaving the deep fascia attached to the gluteus maximus. Large tumors of the buttock should be exposed through the subcutaneous flap despite the possibility of secondary postoperative flap necrosis. The fascia is left attached to the side of the tumor to avoid contamination. (D) The gross specimen following resection. Arrows indicate the gross tumor within the gluteus maximus muscle. This demonstrates that the gluteus maximus is a good compartment to perform wide excision, otherwise termed compartmental resection. The sciatic nerve, the closest significant structure, is often displaced but rarely involved by tumor.

SURGICAL TECHNIQUE

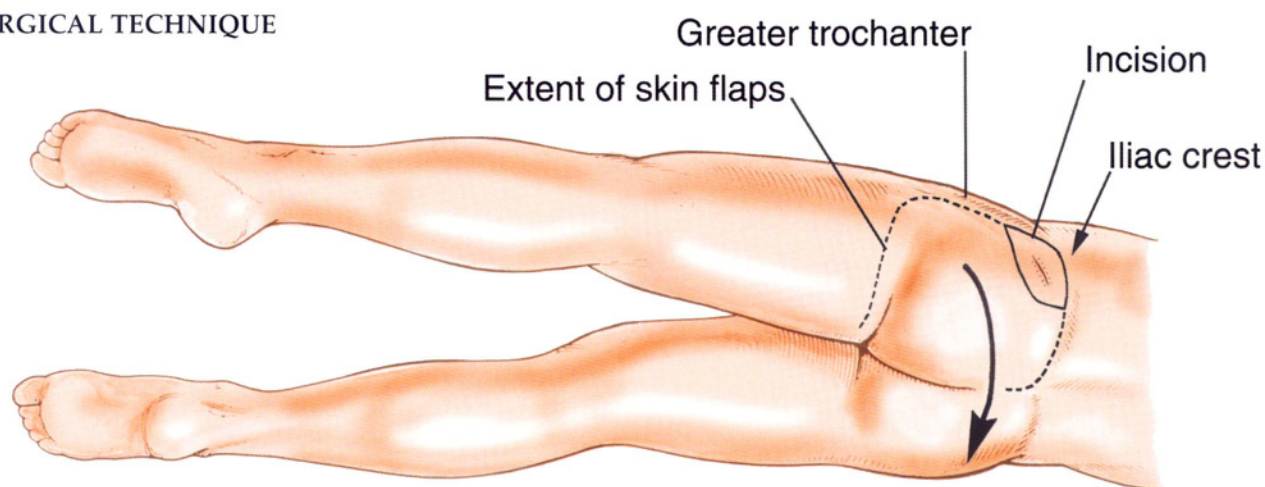


Figure 12.5 Position and incision. A lateral position is utilized. The affected extremity is prepped free from the abdominal wall to the foot. The incision extends along the iliac crest and encompasses the biopsy site by 2–3 cm and then extends along the greater trochanter and along the gluteus maximus skinfold. This incision permits wide excision of the underlying gluteus maximus muscle and early exploration and preservation of the sciatic nerve. If the tumor is unresectable, an anterior flap hemipelvectomy is required.

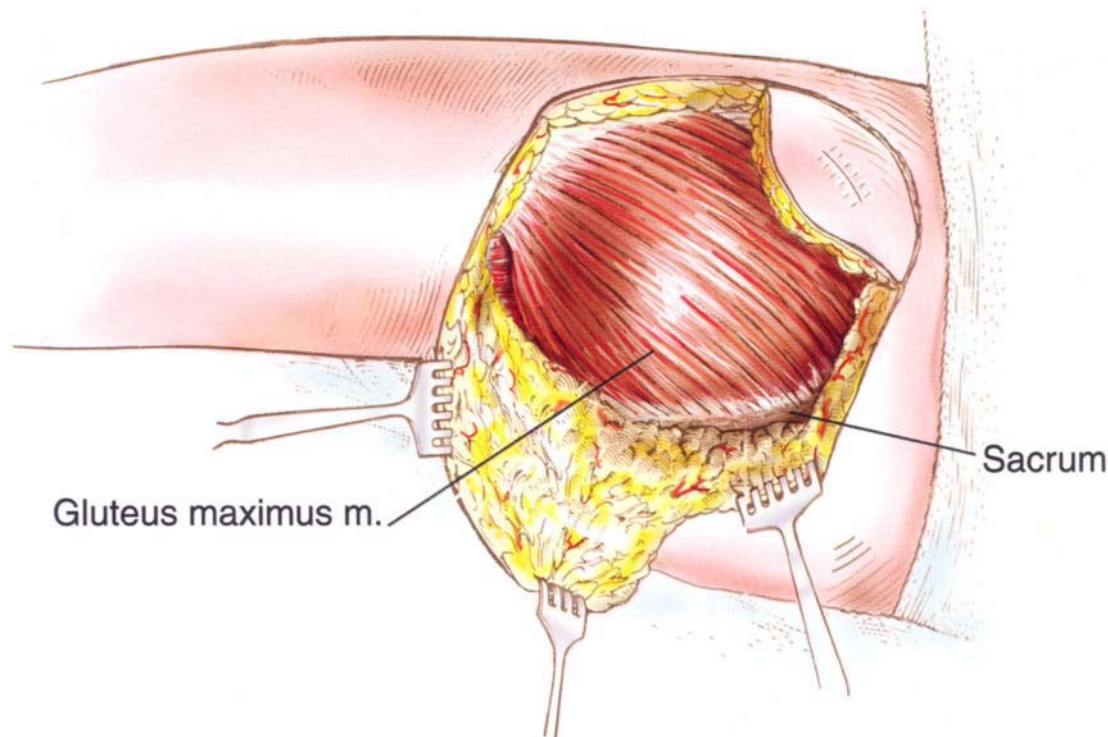


Figure 12.6 Exposure. A fasciocutaneous flap is elevated and dissected with the electrocautery toward the origin of the gluteus maximus muscle (from the sacrum). This permits exposure of the entire gluteus maximus muscle. The biopsy site is left en-bloc with the gluteus maximus muscle. If the tumor is extremely large, then only a subcutaneous flap is utilized with the deep fascia remaining on the tumor side.

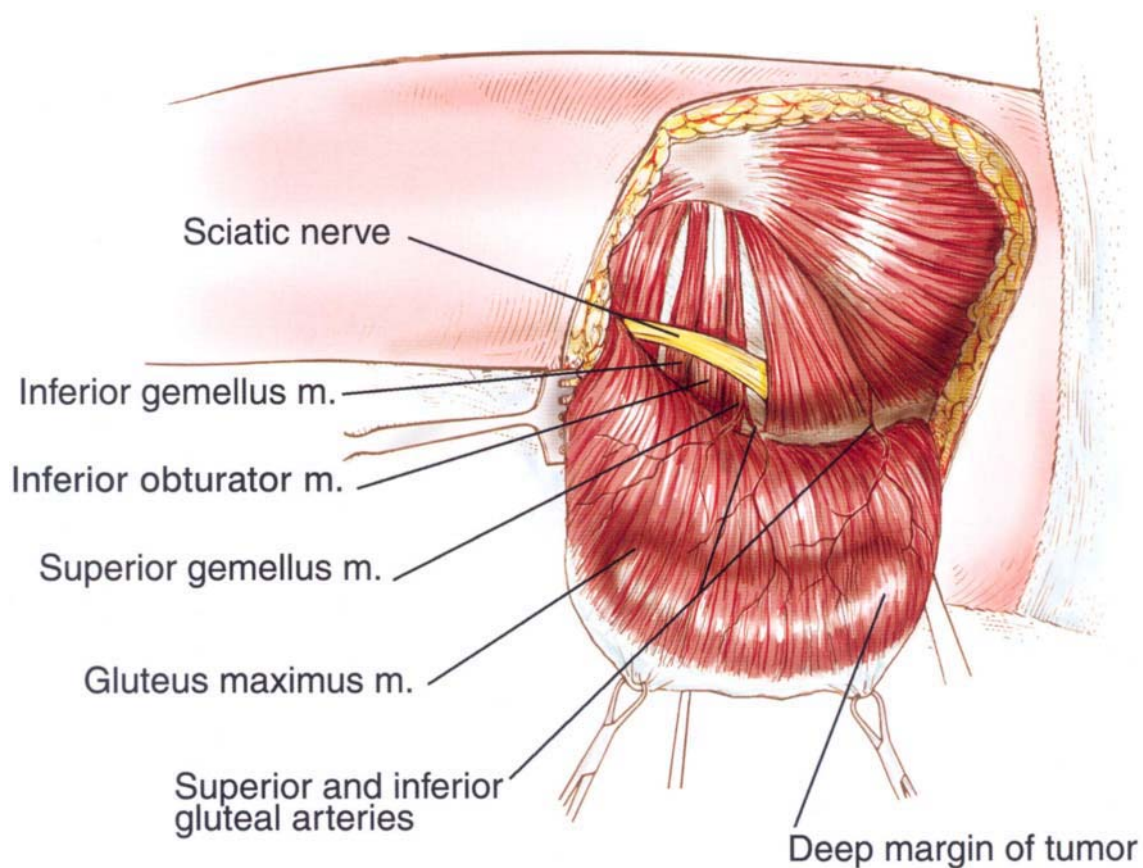


Figure 12.7 Dissection of the gluteus maximus muscle and exploration of the sciatic nerve. The retrogluteal space, consisting of the hip rotators, abductor muscles, and the sciatic nerve, is seen in this illustration. The gluteus maximus is mobilized from inferior along the deep posterior thigh fascia and released from the iliotibial band up to the iliac crest. It is then dissected to its origin along the sacral alar and the sacrotuberous ligament. The sciatic nerve is explored initially by the surgeon placing his hand under the gluteus maximus to ensure that the nerve is separate from the tumor. The inferior and superior gluteal vessels are ligated at its exit from the sciatic notch.

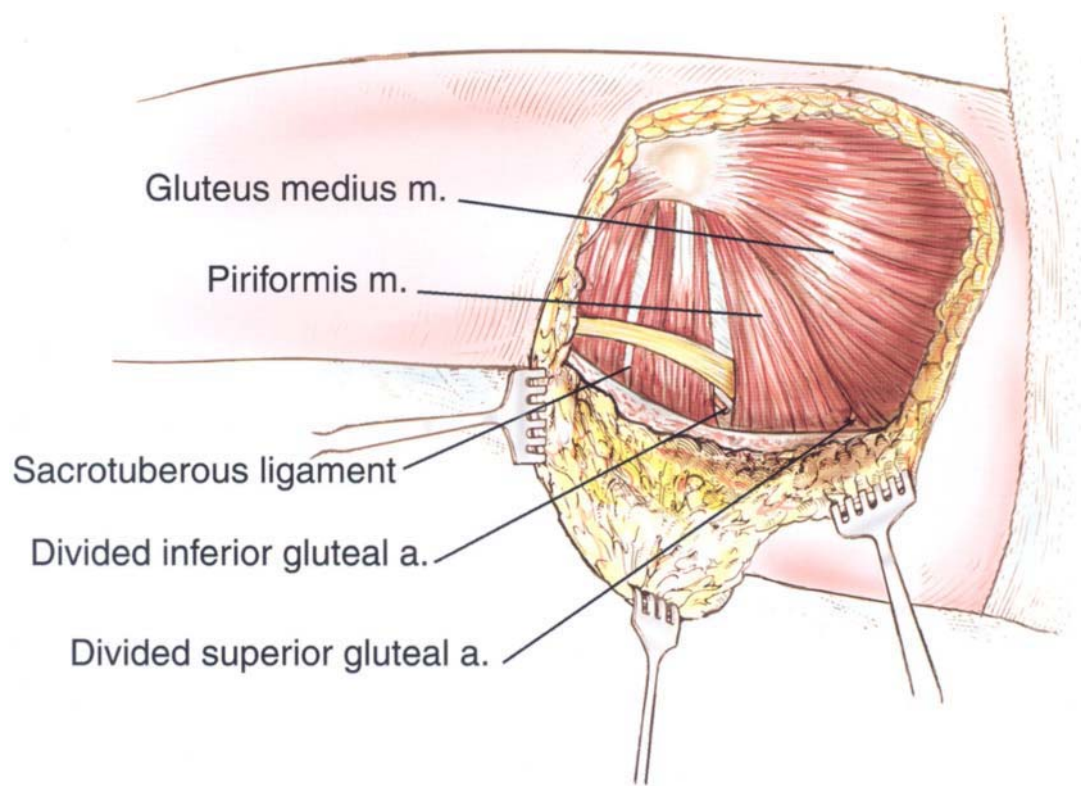


Figure 12.8 Resection. The final surgical maneuver to release the gluteus maximus from the surgical bed is the transection through the origin of its muscle from the sacrotuberous ligament. Care should be taken not to enter the ischiorectal space. The ischium should be palpated, and a hand placed above the ischium and below the gluteus maximus for the release of the tumor specimen.

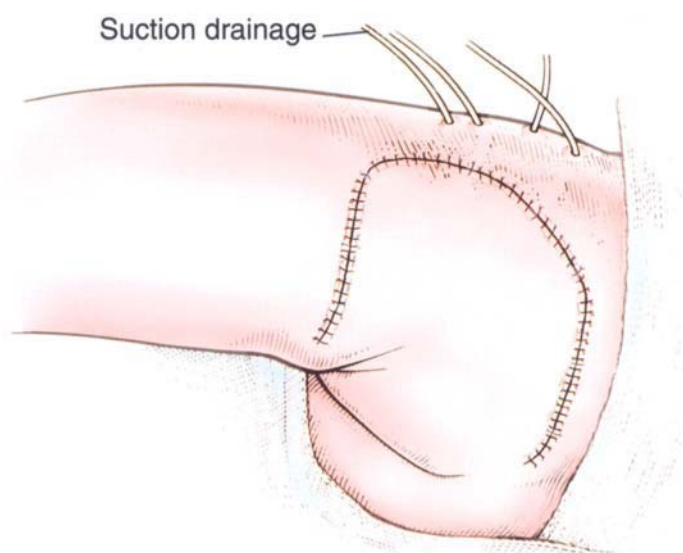


Figure 12.9 Closure. The large posterior fasciocutaneous flap is closed and large suction drainage tubes are utilized. The flap is tacked down to the underlying hip rotator muscles and abductor muscles in order to avoid a postoperative seroma. For 48–72 h a pressure dressing is utilized and the patient lies flat postoperatively.

DISCUSSION

The gluteus maximus is a common area for both low- and high-grade soft-tissue sarcomas. Most often, tumors that arise within the buttocks remain within the substance of the gluteus maximus until they become quite large. Therefore, most low- and high-grade soft-tissue sarcomas of the buttocks can be treated by resection of the gluteus maximus, termed "buttockectomy" or "buttock resection".

The gluteus maximus is a "silent" area for large tumors. The only significant structure that might pose a problem to resection is usually the adjacent sciatic nerve. Fortunately, the sciatic nerve is often protected by a portion of uninvolved gluteus maximus muscle. More recently, if the sciatic nerve is involved by tumor, resection of the sciatic nerve alone or with the tumor mass can be performed while avoiding a hemipelvectomy. The only functional loss following sciatic nerve resection is ankle and foot control that requires an AFO (ankle-foot orthosis). Depending upon the level of the sciatic nerve resection, the first branch to the biceps femoris may be intact. This will permit good knee flexion. Knee flexion is also retained due to the sartorius muscle (femoral nerve innervated), gracilis muscle (obturator nerve innervated), and the two heads of the gastrocnemius that insert across the knee joint.

Traditionally, sarcomas of the gluteal area have been treated by a posterior flap hemipelvectomy. Today most gluteus maximus sarcomas can be treated by a limb-sparing procedure. In the unusual case of recurrent sarcomas of the buttocks, tumor fungation, massive contamination, or extensive tumor involvement of the adjacent structures, an anterior flap hemipelvectomy, as described by Paul Sugarbaker,¹ is recommended. An anterior flap hemipelvectomy (see Chapter 19) is an amputation removing the extremity and all of the buttock structures and skin. The major indications for anterior flap hemipelvectomy are large, unresectable or recurrent buttock sarcomas. Fortunately these are rare occurrences today.

Evaluation of tumors of the buttock must include the structures around the pelvis that might permit intrapelvic extension. Therefore, the ischiorectal space, sciatic notch, and the hip joint area must be closely evaluated. Involvement of any of these structures may indicate the need for an amputation.

The surgical procedure of gluteus maximus resection entails very little morbidity. A large posterior subcutaneous flap is elevated, utilizing Henry's approach to the posterior thigh and buttock area. This permits easy identification of the sciatic nerve distal to the gluteus maximus and permits detachment of the gluteus maximus off of its insertion on the iliotibial band and the femur. With the gluteus maximus detached from its insertion and the large posterior flap developed, the only remaining component of the procedure is to remove the gluteus maximus from its origin along the iliac crest and the sacral alar. It is necessary to perform a meticulous closure of this defect. The most common postoperative complication is the development of a large seroma since there is a large dead space with only a subcutaneous flap on top. We have utilized the quadratus femoris muscle rotated over the sciatic nerve for soft-tissue coverage of the nerve.

Similarly, the piriformis is rotated distally. The flap is carefully tacked down throughout its course in its midportion to eliminate "dead" space. One 20-gauge chest tube and two Jackson-Pratt drains are utilized and the remaining portion of the flap is closed. A compressive dressing is utilized for 72 h.

We prefer the use of induction chemotherapy for high-grade sarcomas. We do not utilize preoperative radiation therapy due to the high risk of flap necrosis. Postoperative radiation therapy is required for high-grade tumors once the flaps are well healed (4–6 weeks postoperatively). Postoperative chemotherapy is given following the radiation therapy.

The advances in limb-sparing surgery have been dramatic and are especially seen in the buttock area where muscle group resections routinely replace the standard hemipelvectomy.

Reference

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Adductor Muscle Group Excision

Martin Malawer and Paul Sugarbaker

OVERVIEW

The adductor muscle group is the second most common site for high- and low-grade soft-tissue sarcomas of the thigh. Liposarcoma is the most common tumor arising within this compartment. Although these tumors often become large prior to clinical detection, limb-sparing resection may be safely performed in 90–95% of patients with adductor tumors. Today, induction chemotherapy, radiation therapy, or both permit a safe compartmental or partial muscle group resection for even the largest tumors. Amputation (modified hemipelvectomy) is required if there is intrapelvic extension, superficial femoral artery and vein involvement, or sciatic notch extension and, in rare cases, palliation.

Preoperative staging studies must evaluate the sartorial canal, pelvic floor, medial hamstrings, ischium, psoas muscle, and hip joint. A limb-sparing procedure begins with dissection and preservation of the superficial femoral artery. The profunda femoris artery is ligated. The adductors are then detached from the femur and from its origin along the inferior and superior pubic rami and ischium. Preservation of the sciatic nerve is necessary. Surgical reconstruction of the defect is performed by transferring the sartorius muscle and the remaining medial hamstrings. Functional loss following resection is minimal.

INTRODUCTION

The adductor compartment is the second most common muscle group involved by soft-tissue sarcomas of the thigh. Tumors arising within the adductor compartment are often extremely large. As they enlarge they often displace the superficial femoral artery and profundus, involve the extrapelvic floor musculature (obturator fascia) and bone (superior and inferior pubic rami and ischium), and even extend extracompartmentally to the medial hamstrings and/or the psoas muscle and the adjacent hip joint. The anatomic characteristics often make resection extremely difficult.

Traditionally, large high-grade soft-tissue sarcomas of the proximal adductor group required an amputation one level above the pelvic ring, i.e., a modified hemipelvectomy. Today, a large majority of these patients may benefit from a limb-sparing procedure (muscle group resection). Wide excision of the involved compartment, followed by postoperative radiation therapy, yields local control rates of 90–95%. Preoperative radiation therapy and resection yield similar results; however, this approach is associated with a very high incidence of wound complications (20–25%). Alternatively, induction chemotherapy has been shown to markedly shrink regional sarcomas and permit resection.

We have examined more than 50 soft-tissue sarcomas following induction chemotherapy. The median tumor necrosis was greater than 90%. On the basis of these findings we conclude that radiation therapy and its associated long-term complications may be avoided if there is greater than 90% tumor necrosis and negative tumor margins. If radiation therapy is required, it is not begun until 3–6 weeks after the wound is completely healed.

ANATOMIC CONSIDERATIONS

The medial (adductor) compartment of the thigh consists of the adductor magnus, the brevis and longus, and the gracilis muscles. All arise from the pelvic floor and the medial aspect of the ipsilateral pelvic ring, symphysis pubis, inferior pubic ramus, ischium, and obturator fascia. They attach distally to the linea aspera and the medial aspect of the distal femur. The adductors are mainly innervated by the obturator artery and nerve. The profunda femoris artery passes through the adductor brevis and travels along the linea aspera. This compartment is best thought of as an inverted funnel – the base being the obturator ring and fascia, the lateral border being the femur and linea aspera, and the tip of the cone being the adductor hiatus (Figure 13.1).

Sartorial Canal

The sartorial canal extends from the femoral triangle to the adductor hiatus, which is an opening of the adductor magnus. The superficial femoral artery passes along the anterior and lateral margin of the entire compartment and forms the lateral border. Most adductor tumors displace the superficial femoral artery (SFA) and vein but rarely directly involve these structures. The profunda femoris artery is often involved and must be ligated as it passes through the adductor brevis.

Pelvic Floor

The bony structures of the pelvic floor are the closest margin for large sarcomas that arise within this muscle group. The obturator artery and nerve, which pass through the obturator fascia, are routinely ligated. Occasionally tumors arising from the pelvic ring require resection of the pelvic floor (Type III pelvic resection) if negative margins are to be obtained in conjunction with a formal adductor group resection. This combination of surgical procedures can be performed as a true limb-sparing procedure in lieu of a hemipelvectomy. Rarely, proximal adductor tumors may extend as a dumb-bell around the ischium into the ischiorectal fossa (space). The possibility of such extension must always be evaluated preoperatively.

Medial Hamstrings and Ischium

The medial hamstrings also take their origin from the ischium. There is no intermuscular septum separating the adductor group from the posterior hamstrings proximally; therefore, extracompartmental extension often occurs between the adductor muscles and the medial hamstrings as these tumors enlarge proximally. Adequate resection may require partial medial hamstring resection.

Sciatic Nerve

The sciatic nerve belongs to the posterior compartment musculature, but as it passes from the buttock to the posterior thigh it is in close apposition to the ischium. Thus, large tumors of the adductor muscles arising near the ischium routinely displace the sciatic nerve as well as extending extracompartmentally. The sciatic nerve must be explored and preserved at the time of surgery. It is usually displaced but is rarely infiltrated by a sarcoma.

The iliopsoas muscle attaches to the lesser trochanter and covers the medial aspect of the hip joint. It is not a

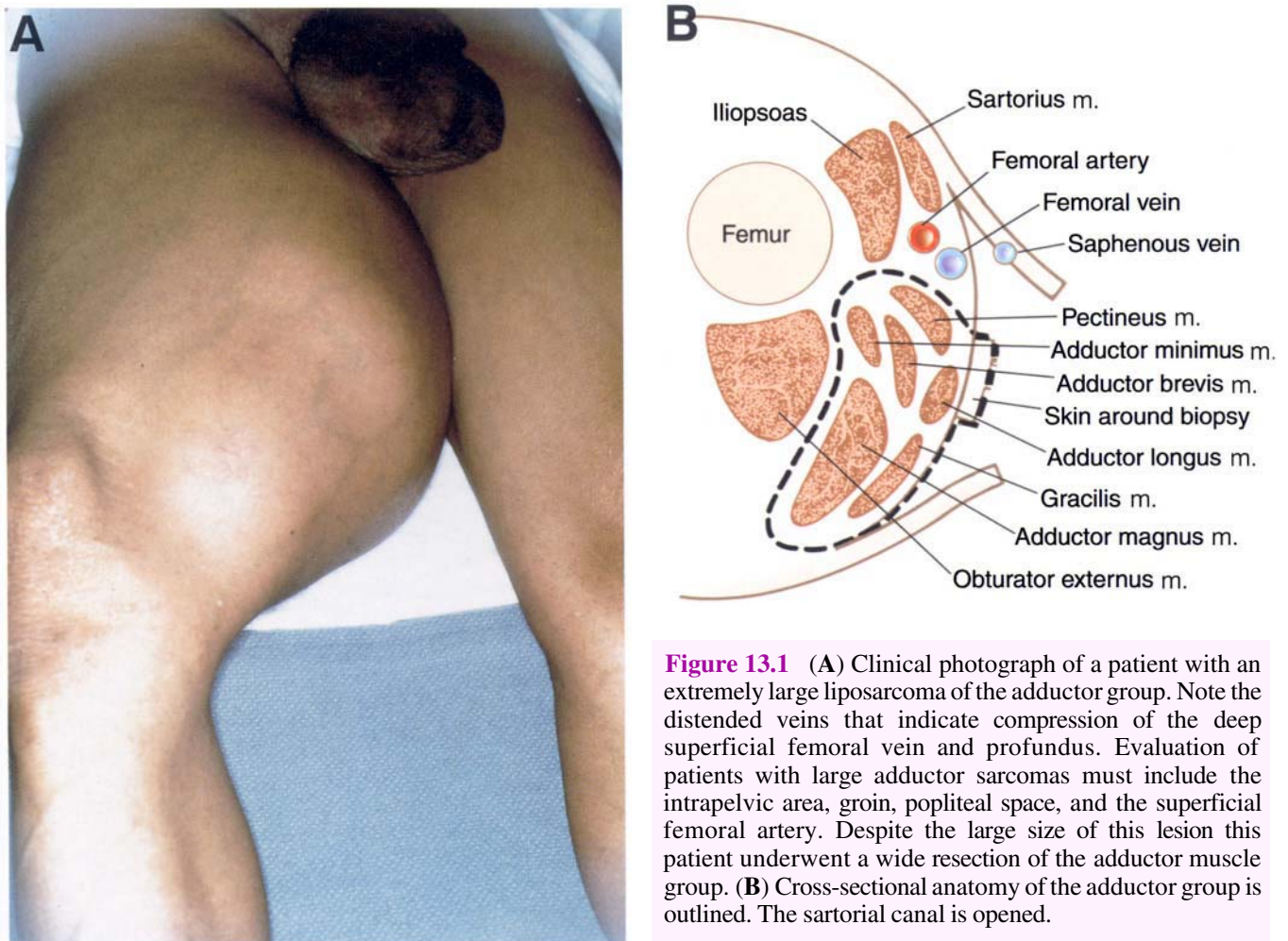


Figure 13.1 (A) Clinical photograph of a patient with an extremely large liposarcoma of the adductor group. Note the distended veins that indicate compression of the deep superficial femoral vein and profundus. Evaluation of patients with large adductor sarcomas must include the intrapelvic area, groin, popliteal space, and the superficial femoral artery. Despite the large size of this lesion this patient underwent a wide resection of the adductor muscle group. (B) Cross-sectional anatomy of the adductor group is outlined. The sartorial canal is opened.

component of the adductor group. Tumors of the adductor brevis and longus may involve the iliopsoas muscle and hip as they enlarge. The iliopsoas and hip capsule must be closely evaluated and removed at the time of resection if involved by tumor.

STAGING STUDIES

Computed Axial Tomography (CAT)/Magnetic Resonance Imaging (MRI)

CAT and MRI are the most useful studies for determining tumor extent (Figures 13.1 and 13.2). Careful evaluation can determine whether a portion of the adductor compartment or the entire compartment must be resected. Both studies are useful to determine bony or soft-tissue extension into the ischiofemoral space, obturator foramen, psoas, and hip capsule, as well as involvement of the proximal medial hamstrings. The sciatic nerve can usually be visualized with these studies.

Bone Scan

Three-phase bone scans of the pelvis and thigh are used to determine pelvic, ischial, and femoral involvement. Increased uptake of bony structures is a contraindication for a traditional compartmental resection, but may indicate whether a combined bony procedure can be performed in order to avoid an amputation.

Biplane Angiography

It is essential to evaluate the relationship of the SFA and profunda femoris artery to the tumor mass (Figure 13.3). The profundus is often ligated when one is performing an adductor muscle group resection. It is important to ascertain whether the superficial femoral artery is patent, especially in older patients. In such individuals the SFA may be completely occluded because of peripheral vascular disease. In such a case,

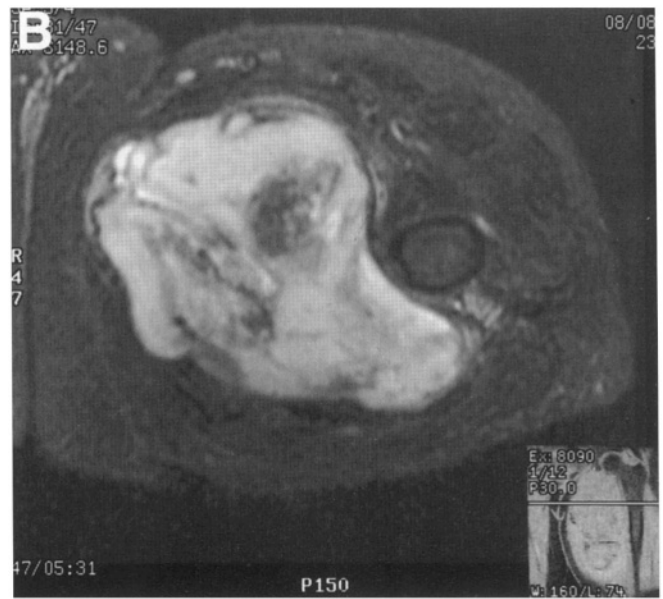


Figure 13.2 Staging studies for large adductor group tumors. (A) Coronal T1 weighted MRI scan of the thigh. Note the large mass (arrows) involving the entire adductor muscle group that is approaching the obturator fascia (pelvic floor) and the hip joint. Note that there is no intrapelvic extension. (B) Axial T2 weighted MRI scan showing large adductor group tumor involving the adductor muscles and displacing the vastus medialis muscle and the superficial femoral artery. There is also extension to and displacement of the gluteal muscles. Large adductor tumors of the proximal thigh often extend into the retrogluteal or hamstring compartments. Low-grade tumors are generally resected with negative margins. (C) Angiography is routinely performed for all adductor group tumors. The superficial femoral artery is often displaced (large black arrows) but almost never involved directly by tumor due to the thick fascial border of the sartorial canal. The profunda vessel is routinely ligated during the dissection as it passes along the adductor longus muscle (see text).

only the profunda artery supplies the lower extremity and it must be preserved. Alternatively, a vascular bypass graft can be performed prior to tumor resection. Ligation of the profunda artery without a patent SFA will lead to a nonviable extremity.

BIOPSY

All biopsy sites should be in line with the anticipated incision for surgical resection. In general, the incision should be parallel to the inferior border of the sartorial canal (Figure 13.1B). A large medial flap based posteriorly is required for the definitive resection. Thus, the biopsy site should be longitudinal and parallel to

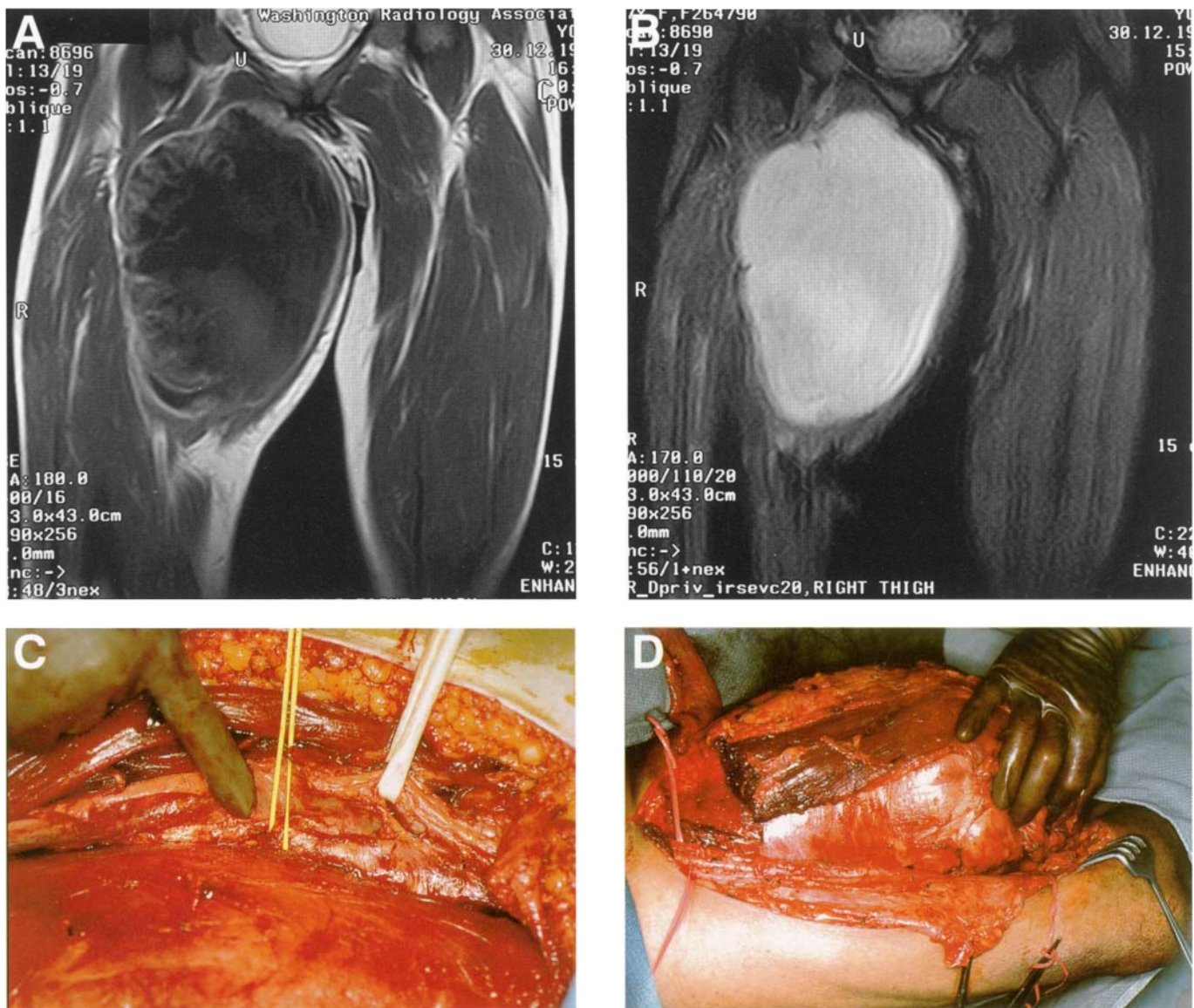


Figure 13.3 (A) Large adductor tumor not involving the pelvic fossa or the hip joint showing significant hemorrhagic necrosis. This occurred following induction chemotherapy. (B) T2 weighted MRI scan showing no evidence of intrapelvic extension. The tumor is located proximally to the thigh with displacement of the superficial femoral artery. (C) Intraoperative photograph demonstrating the exploration and dissection of the entire length of the entire superficial femoral artery from the femoral triangle to the adductor hiatus. The profundus is ligated and the adductor muscles are released from their origin on the distal femur. (D) Intraoperative photograph demonstrating the mobilization of the adductor tumor within the adductor muscle group covered by normal muscle that has been distended as well as the deep fascia of the sartorial canal that is utilized as a border between the tumor and the superficial femoral artery. This is a constant finding that permits safe resection of most adductor tumors. The final step of the surgical procedure is the release of the adductors off of the femur and the obturator fascia (see text).

the sartorial canal. Multiple core biopsies may be taken through a single puncture wound. The biopsy should avoid contaminating the sartorial canal, popliteal space, hip area, pelvic floor, sciatic nerve, and posterior compartment. Diagnostic tissue can easily be obtained from

large tumors in this area. Fine-needle aspiration is usually not utilized for soft-tissue sarcomas. An open incisional biopsy is rarely required. If one has been performed, the biopsy site and all contaminated tissue must be removed en-bloc when the tumor is resected.

INDICATIONS AND CONTRAINDICATIONS TO LIMB-SPARING SURGERY

Approximately 90–100% of most high-grade soft-tissue sarcomas and almost all low-grade sarcomas of the adductor group can be safely resected. Today, amputation is rarely required. There are, however, several contraindications to limb-sparing surgery. In general, a combination of several contraindications is required, most of which are related to extremely large tumors. We recommend induction chemotherapy and repeat staging studies prior to a definitive decision regarding amputation.

Contraindications to limb-sparing surgery include the following:

1. *Major neurovascular involvement.* Direct tumor involvement of the superficial femoral artery within the sartorial canal may occur in rare cases. A vascular graft may be considered, to salvage the extremity.
2. *Pelvic floor involvement.* Tumor extension to the pelvic floor, obturator foramen, and, especially, the ischio-rectal fossa makes resection difficult.
3. *Extensive extracompartmental extension.* Tumor extension to the hip joint, groin, and/or posterior compartment often eliminates a limb-sparing option in patients with extremely large tumors.
4. *Palliation.* Palliation for local recurrence following radiation therapy or failed limb-sparing surgery usually requires a hemipelvectomy, especially in a patient with infection, hemorrhage, or fungation.

SURGICAL GUIDELINES

The surgical guidelines and techniques of complete or partial adductor muscle group resections are summarized:

1. The SFA and vein are initially explored within the sartorial canal, from the femoral triangle to the adductor hiatus. The vessels must be free of tumor. If the tumor extends into the popliteal space the popliteal artery and vein are explored and preserved.
2. Large posteromedial flaps are elevated to expose all resection planes. The resection planes must leave a wide margin and a normal muscle cuff in all directions around the tumor. Portions of the medial hamstrings may have to be removed if the tumor extends proximally.
3. The sciatic nerve is explored early and must be free of tumor and preserved.
4. The pelvic floor and ischium are explored. If involved by tumor, they must be resected either intra- or extrapelvically.
5. The sartorius muscle is preserved and rotated distally to close over the exposed femoral vessels prior to skin closure. The medial hamstrings are rotated anteriorly to cover the femur and popliteal space.
6. A 28-gauge chest tube is utilized to drain the surgical dead space in order to avoid postoperative hematomas. An abduction brace is used for 3–4 weeks postoperatively to prevent abduction and secondary wound dehiscence, especially for the perineal portion of the incision.

SURGICAL TECHNIQUE

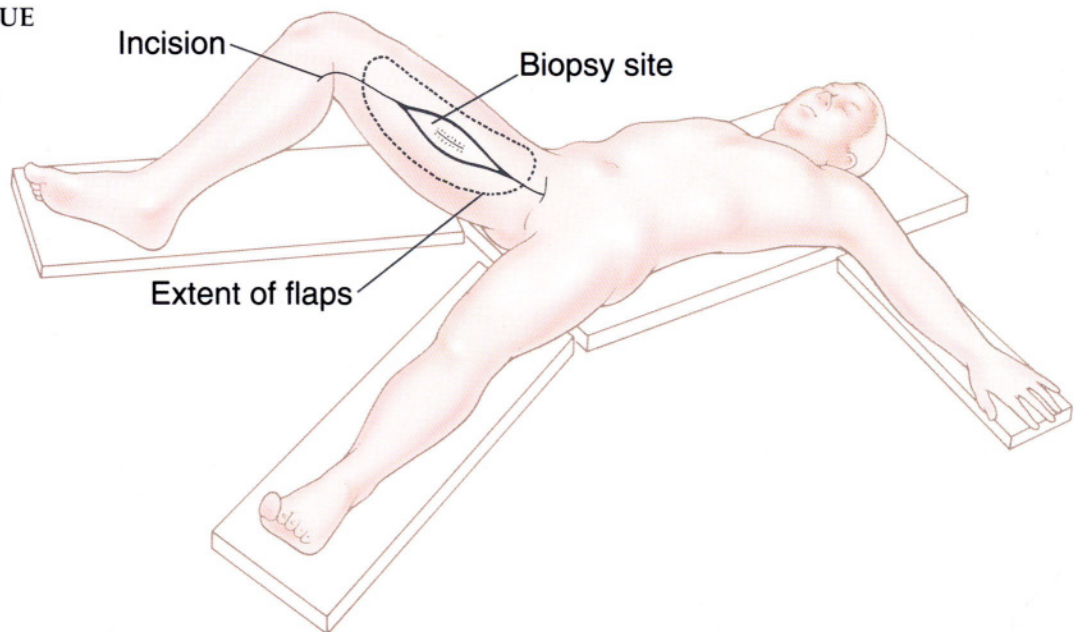


Figure 13.4 Incision. The incision extends from the proximal border of the inguinal region just inferior to the sartorius muscle and parallels the muscle to the posteromedial aspect of the knee. It includes the old biopsy site. This incision permits both large anterior and posterior flaps to be developed in order to visualize the vastus medialis, the sartorial canal, and the entire adductor compartment. The incision can be extended to expose the popliteal space medially if required. The superior extent may have to be "T'd" along the border of the inferior pubic ramus if there is a large soft-tissue component extending to the obturator fossa and ischium.

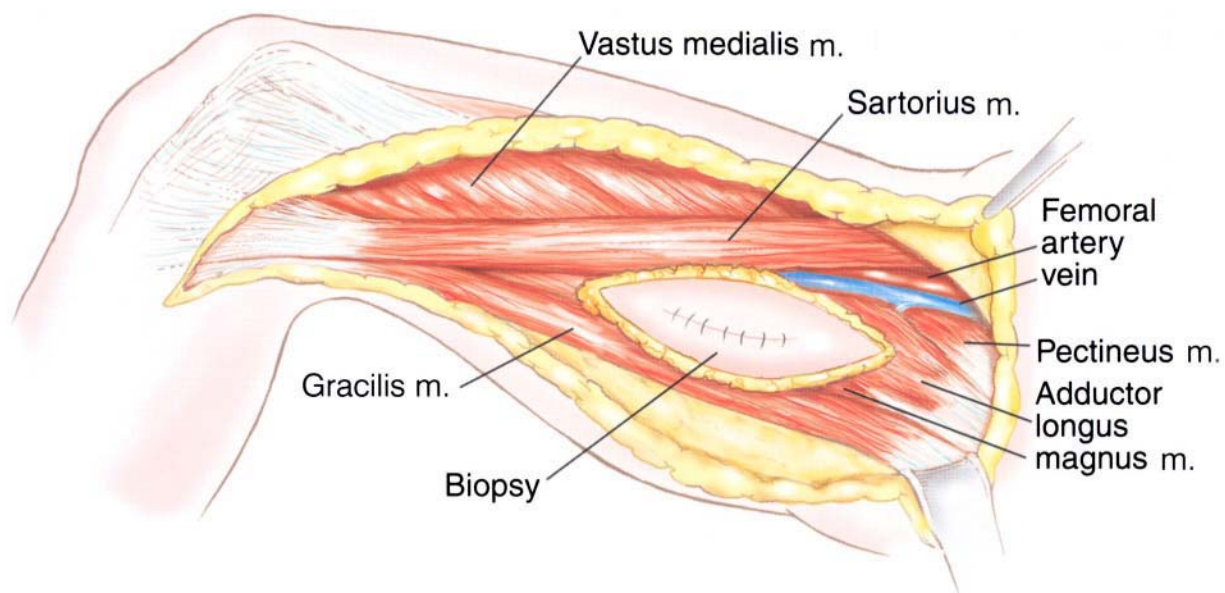


Figure 13.5 Exposure. Large anterior and posterior fasciocutaneous flaps are elevated and retracted anteriorly to expose the vastus medialis and the sartorial canal and posteriorly to the lower edge of the adductor muscle group. If necessary, the incision "T"s along the inferior pubic ramus to expose the proximal portion of the posterior hamstring compartment for large tumors of the proximal region. Note that the biopsy site is left en-bloc with the underlying adductor muscles. The sartorius muscle is the key to the dissection of the entire muscle group. The sartorial canal is opened proximally to identify the common femoral artery and vein prior to ligation of the profundus vessels. The muscles are detached from their origin (superior and inferior pubic rami) and along the obturator foramen. The obturator vessels are ligated and transected. The dissection continues from proximal to distal. The profundus femoral vessels are usually ligated and transected.

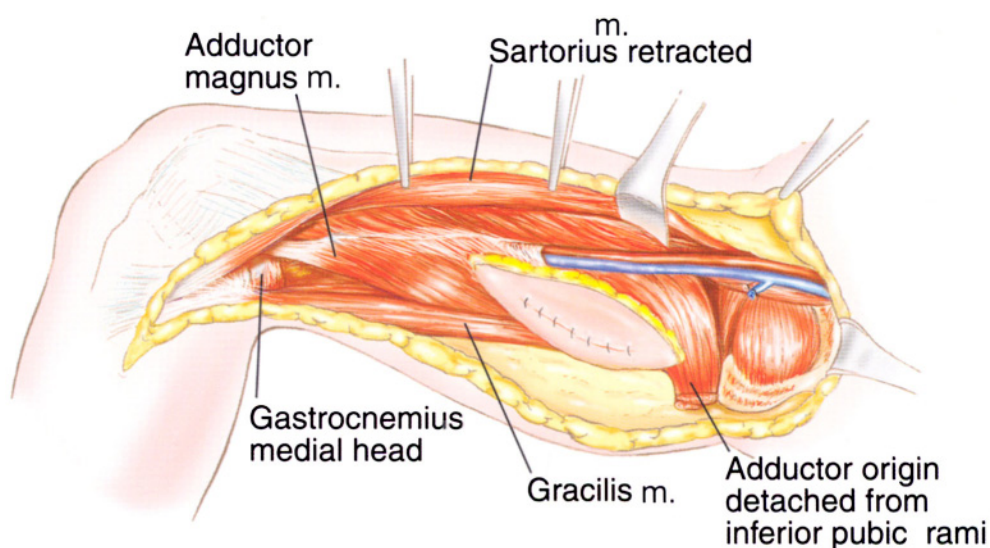


Figure 13.6 Exploration. The sartorial canal is mobilized along the sartorius muscle. The common femoral artery and vein and profunda femoral artery and vein are identified, as well as the popliteal artery and vein as they exit the adductor hiatus by the knee joint. Care must be taken to identify the profunda and common femoral artery and vein prior to ligation of the profundus vessels. The muscles are detached from their origin (superior and inferior pubic rami) and along the obturator foramen. The obturator vessels are ligated and transected. The dissection continues from proximal to distal. The profundus femoral vessels are usually ligated and transected.

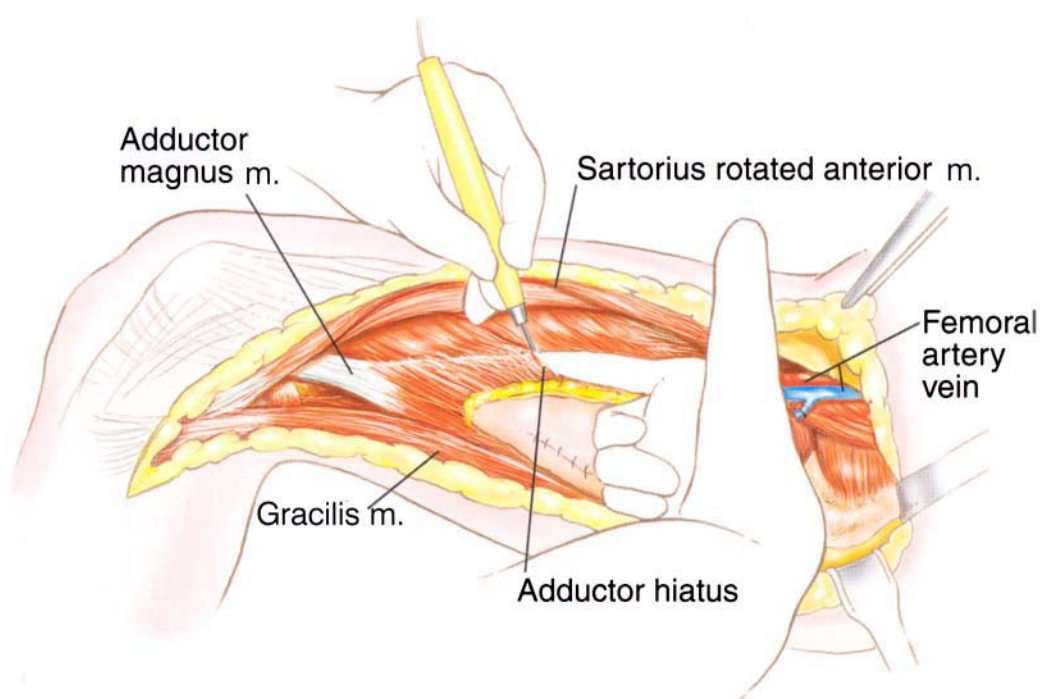


Figure 13.7 Release of adductor muscles from insertion. The adductor magnus and longus are detached from their insertions on the femur throughout its length to the adductor hiatus. The adductor magnus tendon is then transected distally. A finger is inserted into the adductor hiatus in order to guide the cautery and protect the underlying vessels.

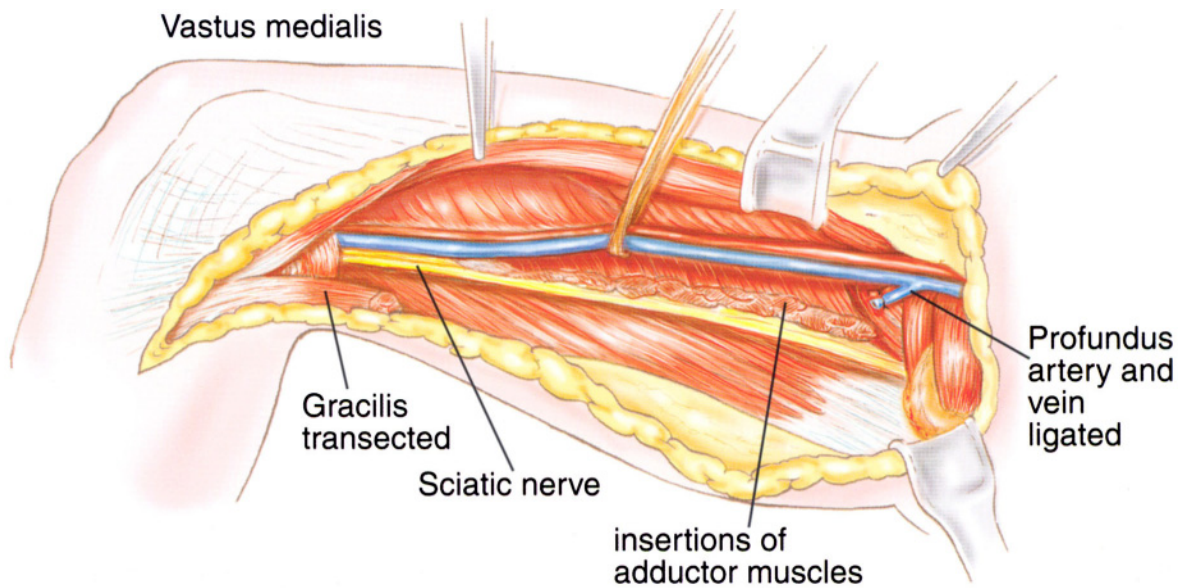


Figure 13.8 Completion of tumor removal. The remaining structures to be transected are the insertions onto the distal femur, as well as portions of the gracilis muscle if required. The entire tumor is then removed and the wound is inspected. The SFA and vein are inspected for any leaks. The cut edge of the muscles along the femur may be oversewn for hemostasis. If there is a large adductor tumor, occasionally a portion of the proximal medial hamstrings must also be removed en-bloc.

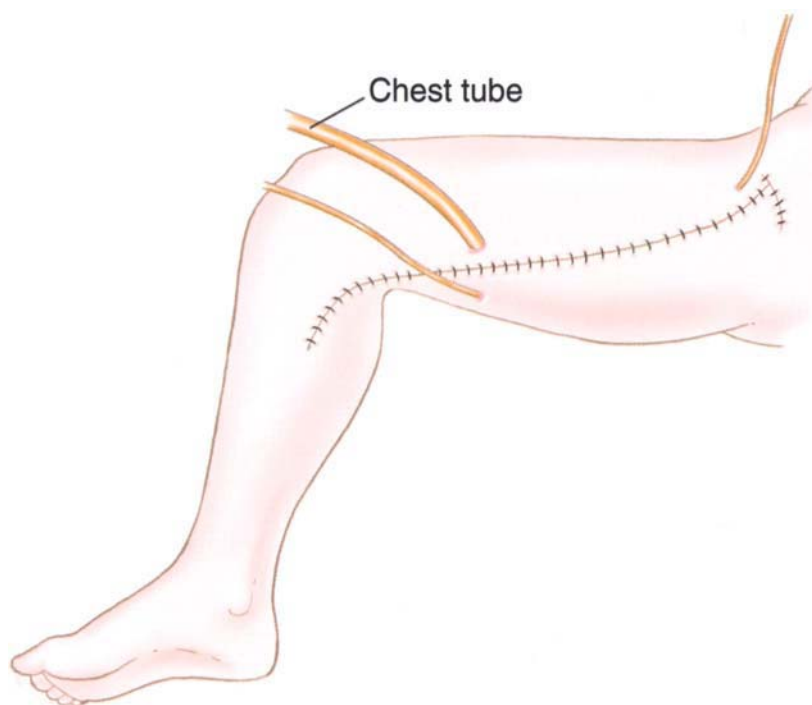


Figure 13.9 Closure. The incision is closed with interrupted layers of sutures. A large 28-gauge chest tube, as well as smaller suction catheters, are utilized to prevent a postoperative seroma. Note a small "T" was utilized proximally in order to develop a flap posteriorly to reach the level of the ischium.

DISCUSSION

Most soft-tissue sarcomas arising within the adductor muscle group can be safely resected by complete or partial muscle group resection. This chapter describes in detail the anatomic constraints, indications, and techniques for such a procedure. Limb-sparing surgery for adductor group tumors has a 90–95% chance of local control. Less than 5–10% of all adductor tumors require an amputation. A modified hemipelvectomy may, however, be required in select circumstances.

Traditionally, large high-grade soft-tissue sarcomas of the adductors – especially those adjacent to the pelvic floor, hip joint, or groin – were treated by an amputation above the pelvic ring, i.e. a modified hemipelvectomy. This operation removes all the tissues and structures at high risk of local recurrence. A modified hemipelvectomy preserves a portion of the ilium and the gluteus maximus so as to permit a myocutaneous closure. If the gluteal region had been contaminated, a classic hemipelvectomy (i.e. through the sacroiliac joint), was

performed. Unfortunately, amputations are still required today, solely because of inadequate or poorly planned biopsies.

The various surgical strategies that have been developed – induction chemotherapy, regional infusion, and/or pre-or postoperative radiation therapy – make limb-sparing surgery very safe. Most patients have an excellent functional result, with minimal loss of adductor strength.

The key to success in adductor group muscle resections is careful preoperative surgical staging of the patient and the tumor, evaluation of the superficial femoral artery, evaluation of the close anatomic restraints (the pelvic floor, sciatic nerve, and hip joint), and surgical resection of all involved structures. The reconstruction is relatively simple, involving closure of the sartorial muscle over the superficial femoral vessels. Adduction is maintained by the medial hamstring and the gluteus maximus muscles. A short course of rehabilitation with an abductor brace permits the patient to resume a normal life.

14

Quadriceps Muscle Group Excision

Martin Malawer and Paul Sugarbaker

OVERVIEW

The quadriceps muscle group is the most common site for extremity soft-tissue sarcomas. The most common sarcomas at this site are liposarcomas, malignant fibrohistiocytomas, and leiomyosarcomas. Although tumors of the anterior thigh can be extremely large prior to diagnosis, approximately 95% of these lesions may be resected. Today, resections of the anterior thigh compartment are extremely safe and reliable, and the reconstructions produce good functional results.

The quadriceps group consists of four muscles, only a portion of which may be required to be resected. When resection of the entire quadriceps muscle group is required, the defect may be reconstructed by centralization of the biceps femoris and sartorius muscles. Careful preoperative evaluation of the femoral triangle, inguinal ligament, groin, superficial femoral artery, and underlying femur is essential to surgery.

There are several treatment strategies for high-grade soft-tissue sarcomas. We prefer induction chemotherapy followed by resection. Postoperative radiation therapy is utilized only if there is less than 90% tumor necrosis or a close surgical margin. The most common indications for amputation (i.e. modified hemipelvectomy) are large tumors with extracompartmental extension into the adductor and hamstring musculature; tumors with intrapelvic extension through the femoral triangle and inguinal ligament; large fungating tumors; and massive contamination, with or without infection.

INTRODUCTION

The quadriceps muscle group (anterior thigh musculature) is the most common anatomic site of extremity soft-tissue sarcomas (Figure 14.1). Approximately 60% of all extremity soft-tissue sarcomas arise within one of the muscles of this group. Most of our surgical experience with extremity soft-tissue sarcomas over the past several decades has been obtained in treating tumors of the anterior thigh.

Pack and Ariel, in their seven-volume textbook on the treatment of cancer, described muscle group resections for soft-tissue sarcomas in lieu of amputations.¹ They coined the term "muscle group" resection. Enneking *et al.*² explained the biological and anatomic basis and growth patterns of soft-tissue sarcomas of the extremities in the 1970s. The concepts elucidated by Enneking would ultimately permit muscle group resections. Enneking emphasized that most sarcomas of the extremities arise within a muscle or group of muscles, which he termed a "compartment" (similar to muscle group). He noted that sarcomas tend to grow centrifugally, i.e. they expand (or "balloon") within the fascial borders of their specific compartment. He emphasized that sarcomas rarely will penetrate a transverse fascial border. They will, however, extend proximally and distally within a muscle group, making it necessary surgically to remove the entire compartment to avoid a local recurrence. Enneking differentiated this growth pattern from that of carcinomas, which invade adjacent structures and are not confined by fascial or anatomic borders.

During the 1970s and 1980s Enneking developed the principles of surgical resection and established a surgical staging system and classification that is based on these biological principles. He emphasized that low-grade sarcomas can be resected safely by removing only a portion of a muscle group, as long as there is normal muscle in all directions. Surgery alone for low-grade sarcomas following these principles showed less than 10% local recurrence rate. He noted that when a high-grade soft-tissue sarcoma is treated by resection alone (as long as the entire muscle group is resected) the results were equivalent to those of amputation, i.e. a local recurrence rate of 5–10%). He concluded that a true muscle group resection from insertion to origin was equivalent biologically to an amputation one joint above the lesion.

The tendency of soft-tissue sarcomas to remain within a compartment protected by fascial borders is the biological basis that permits safe muscle group resections. Over the following decades the tendency has been to perform less than a muscle group resection when combined with adjuvant therapy and/or radiation therapy and chemotherapy. Today, less surgery is



Figure 14.1 Clinical appearance of a typical quadriceps mass (arrows). Most tumors of the quadriceps can become quite large. They may involve one or multiple muscles of the quadriceps mechanism.

required than a true muscle group resection for select sarcomas.

This chapter discusses the unique anatomic aspects of the quadriceps muscles, describes the important staging studies for soft-tissue sarcomas that arise at this site, and presents a surgical technique for partial or complete reconstruction of the quadriceps muscle group.

ANATOMIC CONSIDERATIONS

The thigh consists of three muscle groups: the quadriceps (anterior thigh), the adductor muscles (medial thigh); and the hamstring muscle (posterior thigh). The quadriceps muscle group consists of the vastus medialis, vastus lateralis, rectus femoris, and vastus intermedius muscles. Soft-tissue sarcomas may arise in any of the four muscles (i.e. intramuscularly) or between them (i.e. extramuscularly); however, they are intracompartmental. The vastus medialis, lateralis, and intermedius arise from the proximal femur and intermuscular septum and insert onto the patella. Only the rectus femoris arises from the pelvis and also inserts onto the patella.

It is important to note that only the vastus intermedius muscle arises from the surface of the femur and the linea aspera and covers the entire femoral shaft. Thus, the vastus intermedius protects the underlying femur from direct tumor extension by tumors of the other quadriceps muscles. Tumors arising within the vastus intermedius lie on the periosteum of the femur, or extend to the linea aspera. Tumors arising within other portions of the quadriceps generally remain localized to their respective muscle belly and only rarely cross into a second muscle. This anatomically permits partial muscle group (myomectomy) resection for many quadriceps sarcomas.

The medial and lateral intermuscular septum of the thigh separates the anterior thigh muscles from the posterior compartment as well as the medial compartment. The medial intermuscular septum, however, "runs out" proximally; quadriceps tumors may therefore extend into the posterior and medial compartments and make a limb-sparing resection difficult. Similarly, tumors of the posterior thigh and/or the adductor group may extend into the quadriceps group, making resections more difficult.

The anatomic structures that must be evaluated prior to surgery are the superficial femoral artery, the femoral triangle, and the adductor hiatus.

The femoral triangle is the key to resection of the quadriceps muscle group. It is formed by the adductor longus medially, the sartorius muscle laterally, and the inguinal ligament proximally. The pectineus muscle forms the floor of the triangle. A thick fascia covers the roof. The superficial femoral artery and vein pass from below the inguinal ligament through the femoral triangle and into the sartorial canal at the apex. The femoral nerve enters the canal laterally and quickly divides to innervate the quadriceps muscles. The superficial femoral artery and vein pass along the medial wall of the sartorial canal throughout the length of the thigh and are separated from the anterior group (vastus medialis) by a thick fascia, which often permits a safe

resection. The vastus medialis fascia forms a good border for quadriceps resections.

STAGING STUDIES

CAT and MRI

Computed axial tomography (CAT) and magnetic resonance imaging (MRI) are important to determine the extent of soft-tissue sarcomas of the anterior thigh, and which quadriceps muscles are involved (Figure 14.2). Tumors may remain within one muscle or involve several muscles. It is important to identify the relationship of the involved and the underlying femur. If the vastus intermedius is involved by tumor, the adjacent periosteum is always involved as well.

Bone Scan

A three-phase bone scan is useful to determine the proximity of the tumor to the periosteum. Increased periosteal uptake indicates a reactive border or a pseudocapsule. This does not make quadriceps tumors unresectable, but it does indicate that the underlying periosteum must be removed during the surgical procedure. Tumors of the vastus intermedius routinely show increased uptake of the underlying femur. Rarely does tumor extend directly into the bone.

Biplane Angiography

Large tumors of the quadriceps muscle often displace the superficial femoral artery and the profunda femoris artery and vein (Figure 14.3). It is important to determine the anatomic relationship of these vessels to the tumor prior to resection. Large tumors of the proximal thigh may require ligation of the profunda femoris artery and vein; therefore it is important to know prior to surgery whether the superficial artery is patent. This is particularly true in the older patient, in whom the SFA may be occluded because of disease. Superficial femoral artery displacement does not usually indicate direct tumor extension, but if the margin is close or positive, a femoral artery graft can be utilized.

INDICATIONS AND CONTRAINDICATIONS TO LIMB-SPARING RESECTION

Almost all low-grade soft-tissue sarcomas of the anterior thigh may be safely resected by a partial muscle group resection. The large majority of high-grade soft-tissue sarcomas can be resected by partial or total compartmental removal. The contraindications to limb-sparing resection are as follows:

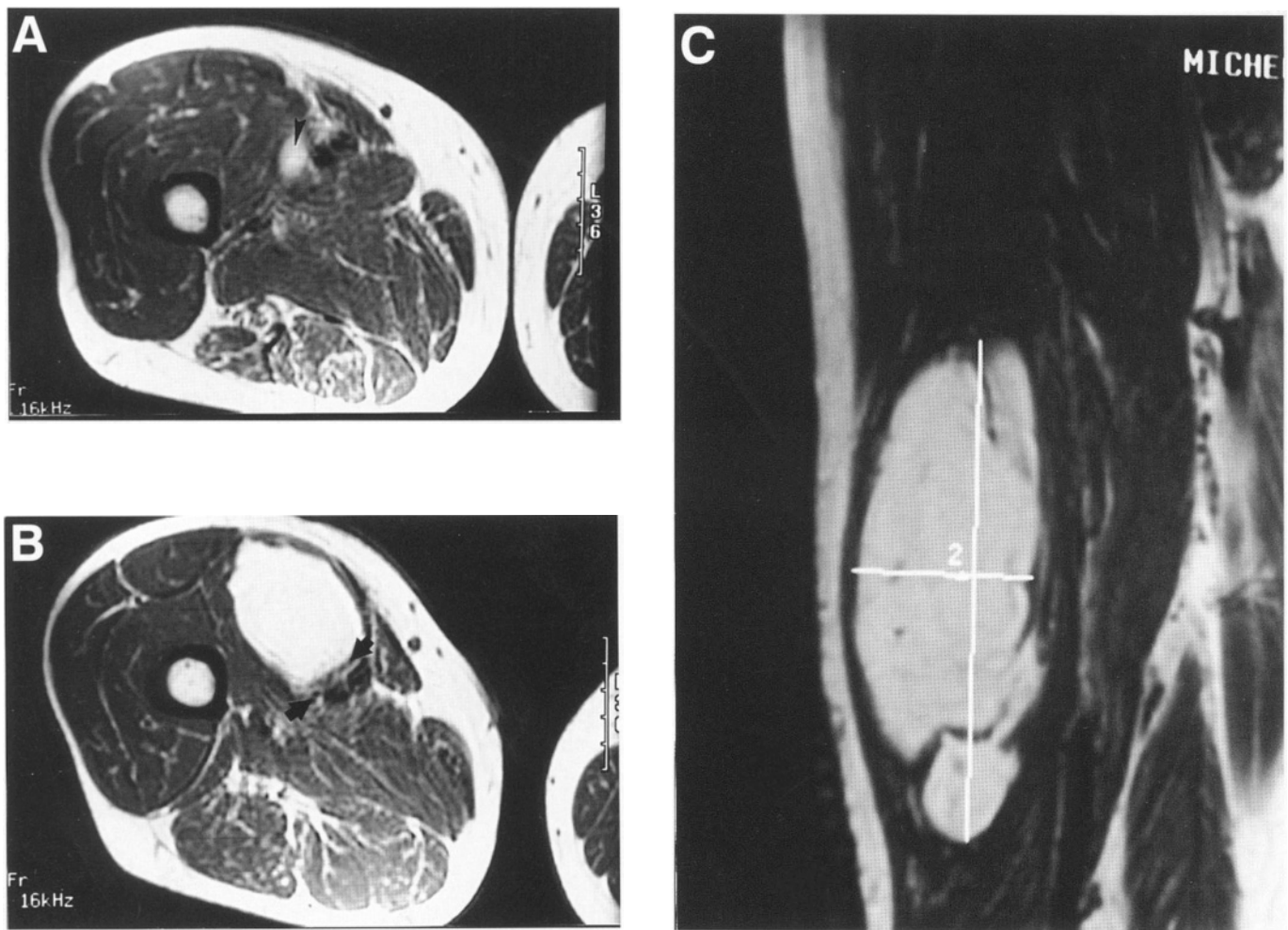


Figure 14.2 MRI evaluation of a quadriceps mass. (A) Axial T1 weighted image. Note the small tumor of the inferior aspect of the vastus medialis adjacent to the superficial femoral artery and vein (small arrow). (B) Axial T1 weighted image of the same patient shows large tumor involvement of the vastus medialis muscle but it is separated from the superficial femoral artery and vein (sartorial canal) by a thick fascial border of the vastus medialis (solid arrows). This fascial usually provides a safe resection margin. (C) Sagittal image of the same tumor (low to intermediate grade liposarcoma) showing almost a separate tumor with a small connection to the primary mass. Liposarcomas characteristically may have multiple lesions within the same muscle belly.

1. *Groin involvement.* Tumors arising or involving the groin and femoral triangle often cannot be reliably resected and may require amputation.
2. *Extracompartmental extension.* In general, a single muscle group permits a viable extremity. If two muscle groups have to be removed, the extremity is probably not salvageable. Large tumors of the anterior thigh may involve the adductor group as well as the posterior muscle group by passing through the linea aspera or the intermuscular septum. In this situation amputation is necessary.
3. *Intrapelvic extension.* On rare occasions, large tumors of the proximal thigh and groin extend below the inguinal ligament into the retroperitoneal space, necessitating amputation.
4. *Superficial femoral artery or common femoral artery involvement.* Most tumors of the quadriceps muscle will displace, but do not invade, the superficial femoral artery or common femoral artery. If there is a minimal margin, resection of the artery with a vascular graft can avoid an amputation. Femoral nerve sacrifice is not a contraindication to resection, because hamstring transfers can restore stability of the lower extremity if the entire muscle group is resected.
5. *Femur involvement.* Large tumors often involve the underlying femur and multiple compartments. This is particularly true of tumors of the vastus intermedius. This combination usually requires an amputation, especially if there is poor response to induction therapy (radiation or chemotherapy).

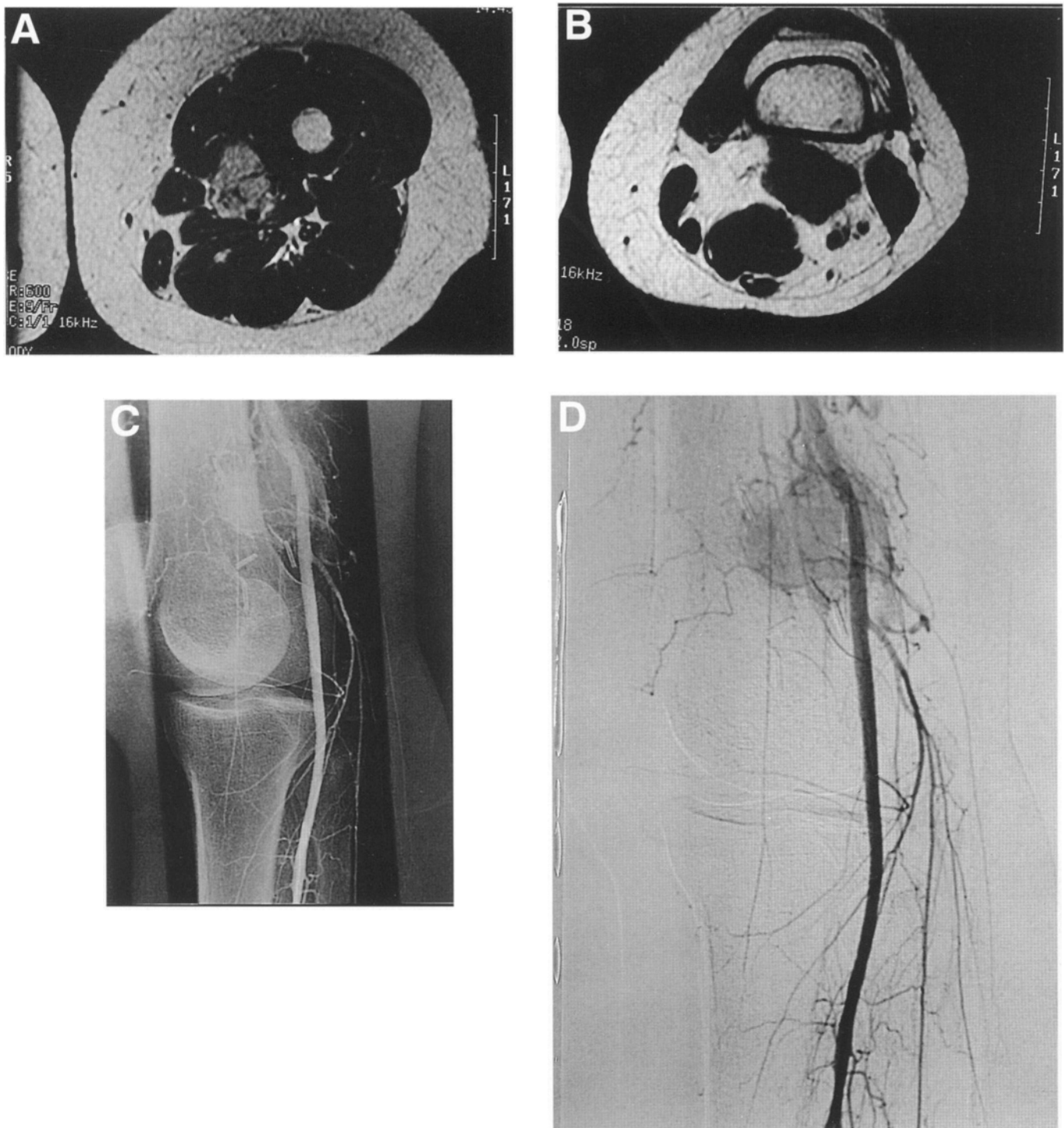


Figure 14.3 Leiomyosarcoma involvement of the sartorial canal and extension distally into the popliteal space. Evaluation of tumors of the thigh must include careful inspection of the sartorial canal and the superficial femoral artery and vein. Tumors arising within the sartorial canal are rare, but often travel superiorly along the anterior thigh below the sartorius muscle and distally into the popliteal space (as shown). (A) Tumor within the sartorial canal. The sartorius helps to orient the location of the lesion. (B) T1 weighted MRI scan through the popliteal space shows tumor extension into the popliteal space. The tumor tracks down the length of the superficial femoral artery and may be located extremely proximally or distally to the original tumor mass. (C) Lateral angiogram of the same tumor showing a tumor blush circumferentially located around the superficial femoral artery. (D) Subtraction angiogram showing tumor blush at the level of the popliteal space and the sartorial canal. This patient was treated by wide excision of the vastus medialis and the sartorial canal along with the superficial femoral artery and vein, and was reconstructed with a long Gore-Tex[®] graft. The tumor arose from the popliteal vein.

6. *Palliation.* Recurrent tumors of the quadriceps, infection, extensive tumor hemorrhage, or extensive contamination from previous surgical procedures may require an amputation.

BIOPSY

The biopsy site should be in line with the potential incision for resection. This incision extends proximally from lateral to the femoral triangle, parallels the sartorial canal, and curves medially over to the adductor hiatus. The biopsy should be over the most prominent portion of the tumor. We recommend core needle biopsy. Multiple samples can be collected from the same puncture site. The femoral triangle, sartorial canal, hip joint, patella, and popliteal space should be avoided to prevent contamination.

SURGICAL GUIDELINES

The guidelines and technique of complete or partial anterior thigh (quadriceps muscle group) resection are:

1. The superficial femoral artery and vein are initially explored throughout the length of the sartorial canal and must be free of tumor.
2. A long midline incision is utilized with large medial and lateral flaps in order to expose the planes of resection (the intermuscular septum).
3. The entire quadriceps muscle group or a portion thereof is resected. If the underlying femur is the closest border, the periosteum can be removed and the underlying bone exposed by utilizing a high-speed burr (Midas). Several millimeters of the outer cortex can be removed; however, the outer cortex itself should not be removed en-bloc. This may not be necessary following induction chemotherapy and/or postoperative radiation therapy. Resection of the outer cortex of the femur poses a substantial risk of fracture following postoperative radiation therapy.
4. The sartorius muscle is usually preserved and utilized to cover the femoral vessels following resection.
5. If no quadriceps muscles remain, a primary transfer of the long head of the biceps, as well as a transfer of the sartorius and gracilis to the patella, should be performed to restore the lost quadriceps power and close the operative dead space.
6. A 28-gauge chest tube is utilized to drain the surgical space and avoid postoperative hematomas.

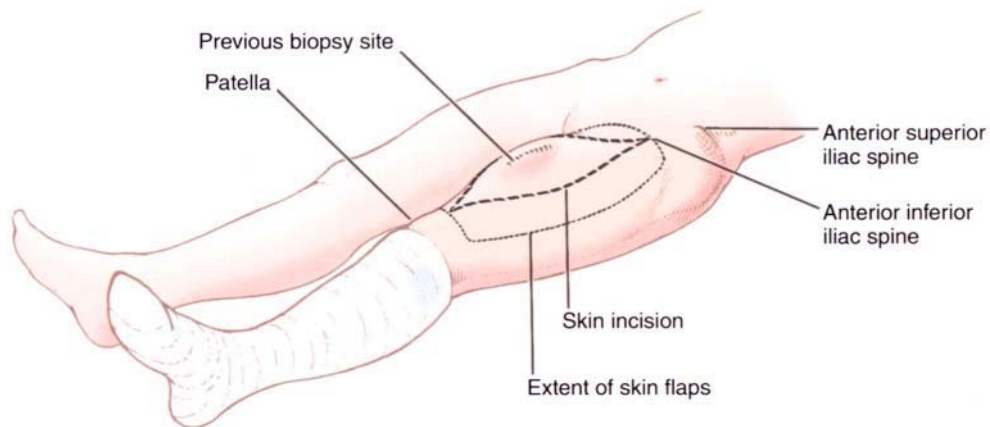


Figure 14.4 Incision. The incision extends longitudinally from the superior inferior iliac spine to the patella. It should be elliptical in configuration and widely encompass the biopsy site. If physical examination or tomography shows that the tumor encroaches on the patella, this bone and its tendon should also be excised. If this clinical situation arises, the incision should be continued over the knee to the tibial tubercle.

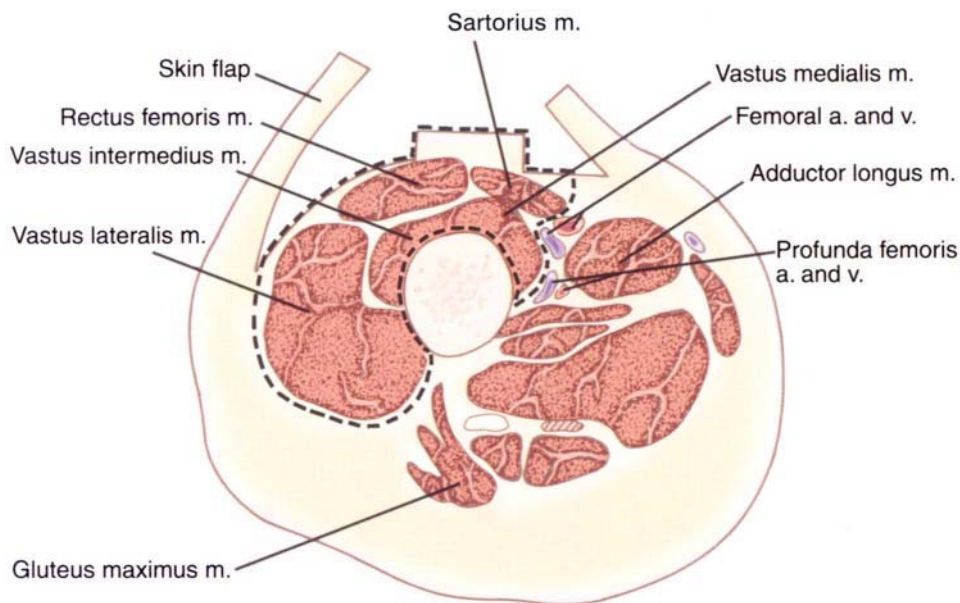


Figure 14.5 Cross-sectional anatomy.

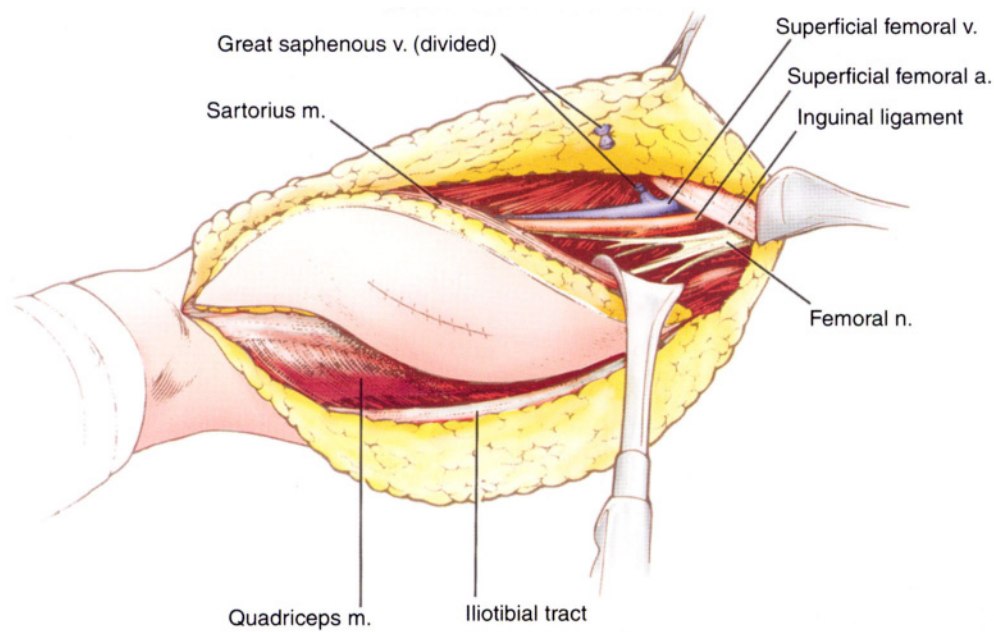


Figure 14.6 Skin flaps. Flaps composed of skin and subcutaneous tissue are made just superficial to the fascia lata. They extend to the adductor muscle group medially and to the greater trochanter and flexor muscles laterally. The saphenous vein is divided as it enters the fossa ovalis. The inguinal ligament and the femoral triangle are uncovered, exposing the common femoral artery and vein and the femoral nerve.

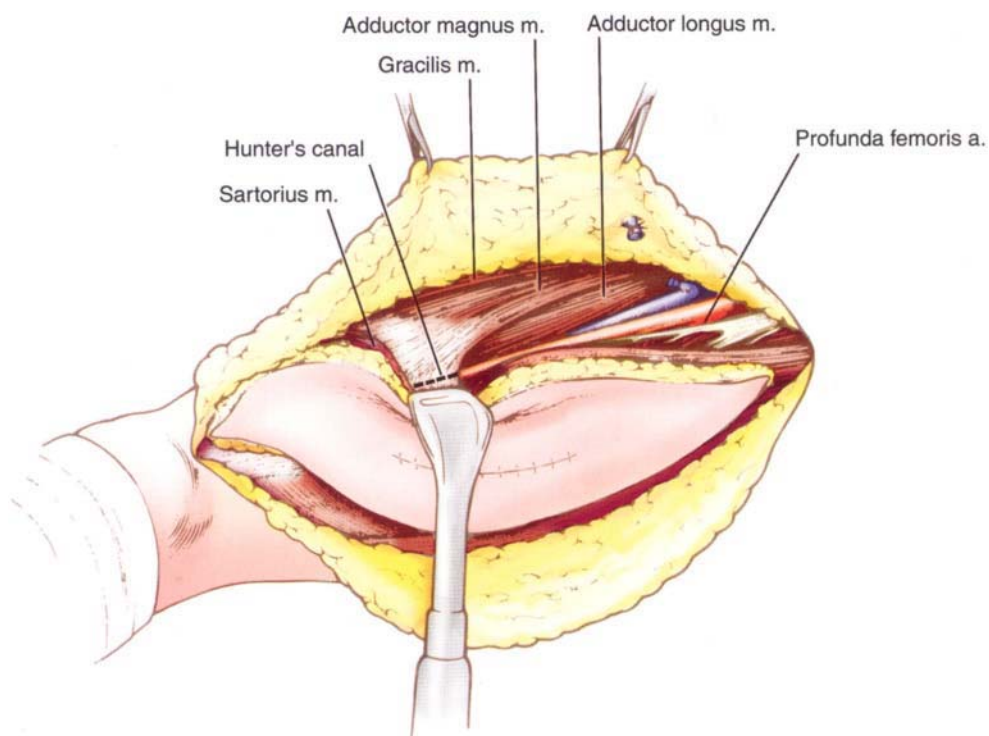


Figure 14.7 Dissection of the superficial femoral vessels. Lateral traction is placed on the quadriceps muscle group so that muscular branches coming from the superficial femoral artery and vein into the quadriceps muscle are exposed. Working from cranial to caudal, these vessels are clamped, divided, and ligated; included are the profunda femoris artery and vein. In the area of Hunter's canal, when strong lateral traction is placed on the sartorius muscle, muscular insertions from the adductor magnus muscle coursing over the superficial femoral artery are identified. These muscle fibers should be divided as they cross the superficial femoral artery.

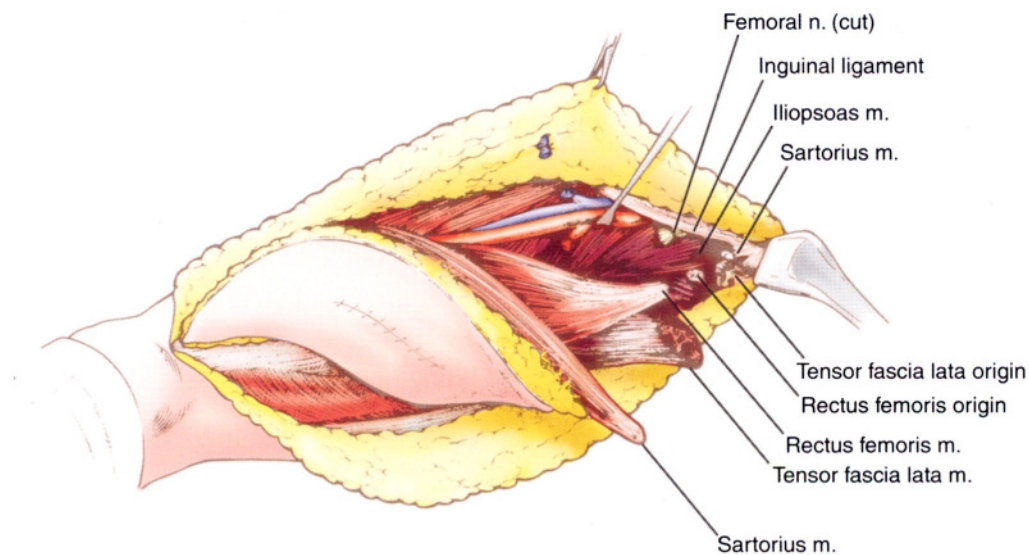


Figure 14.8 Transection of muscle origins on the pelvis. A plane beneath the tensor fascia lata muscle and above the gluteus medius and minimus is identified. By electrocautery the tensor fascia lata muscle is released from its origin on the wing of the ilium. Then the origin of the sartorius muscle on the anterior superior iliac spine is identified and divided. The origin of the rectus femoris muscle on the anterior inferior iliac spine is likewise identified and divided through its tendinous portion.

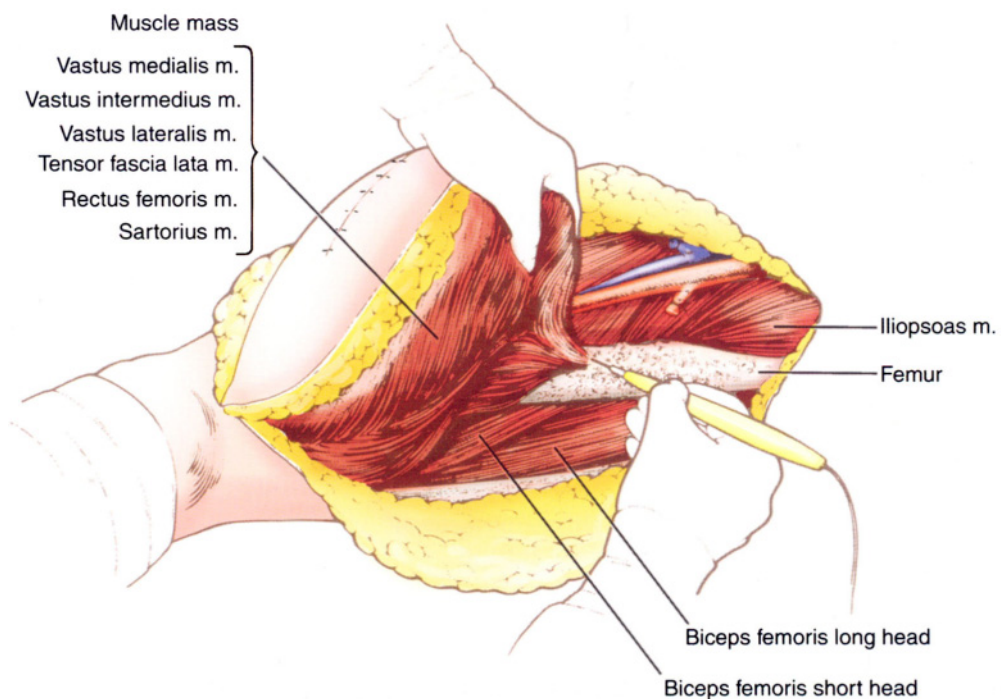


Figure 14.9 Transection of muscle origins on the femur. Origins of the vastus lateralis, vastus intermedius, and vastus medialis on the femur are transected from bone by using electrocautery. Strong upward traction on the muscle group facilitates this dissection.

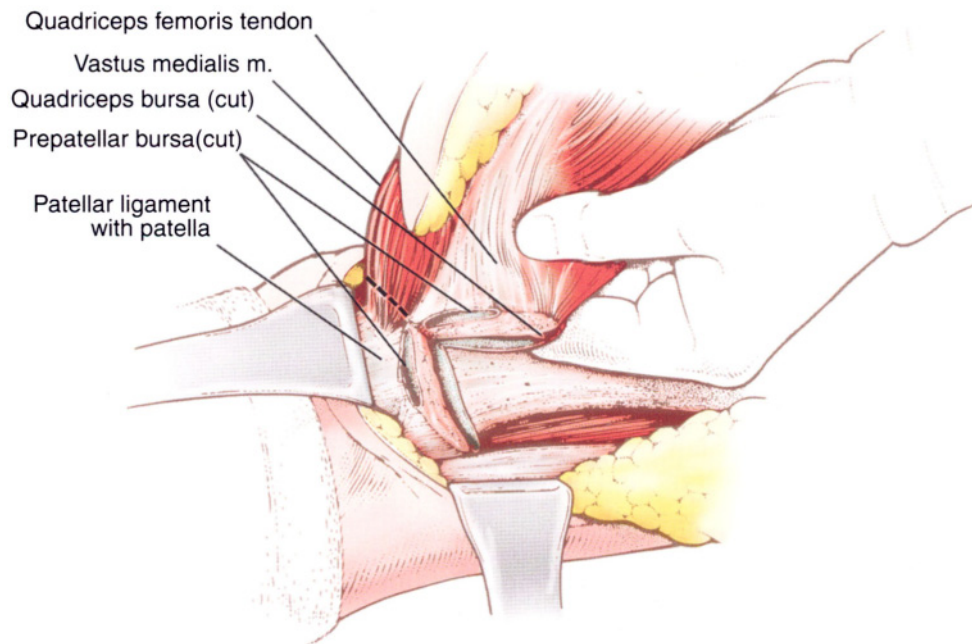


Figure 14.10 Transection of the muscle insertions of the quadriceps muscle. Using strong upward and medial traction on the specimen, insertions of the vastus lateralis, vastus medialis, and rectus femoris into the patellar tendon are divided on the patella bone. The insertion of the vastus medialis into the medial collateral ligament is likewise divided, and the specimen is then free. The dissection site is copiously irrigated, and any bleeding points are secured with ligatures or electrocautery.

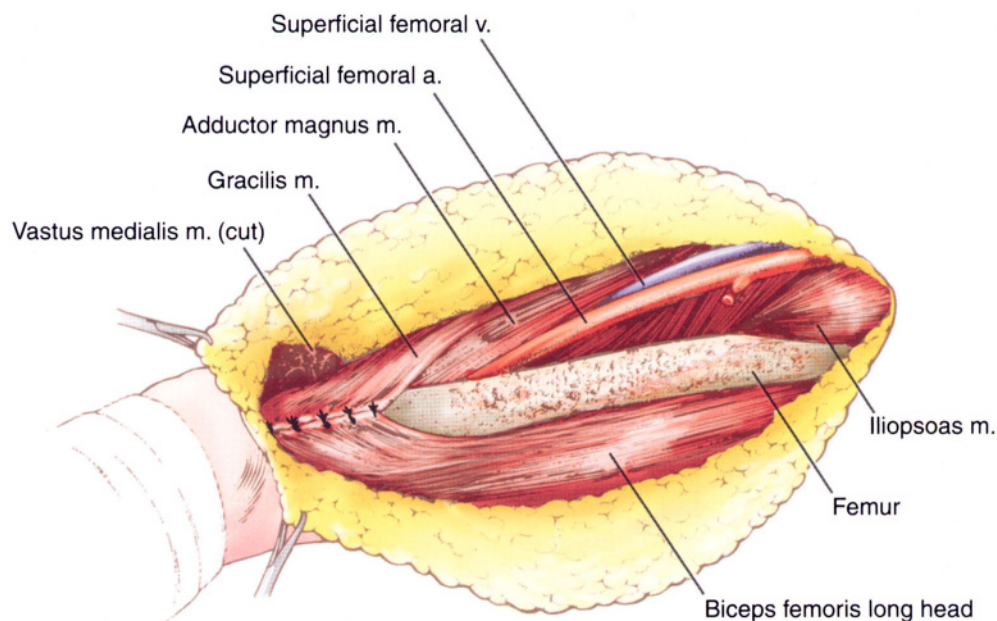


Figure 14.11 Reconstruction. To facilitate rehabilitation by helping to provide stability to the knee, the gracilis and sartorius muscle (if not retracted) medially and the long head of the biceps femoris muscle laterally are transected at their insertions on the tibia and fibula. This transection should be as far distal on the muscle as possible so that a tendinous portion of the muscle is retained on the muscle belly. Then, using heavy nonabsorbable sutures, these two muscles are transplanted onto the patellar tendon. The muscles are transferred anteriorly to the midline so that they cover the distal one-third of the femur.

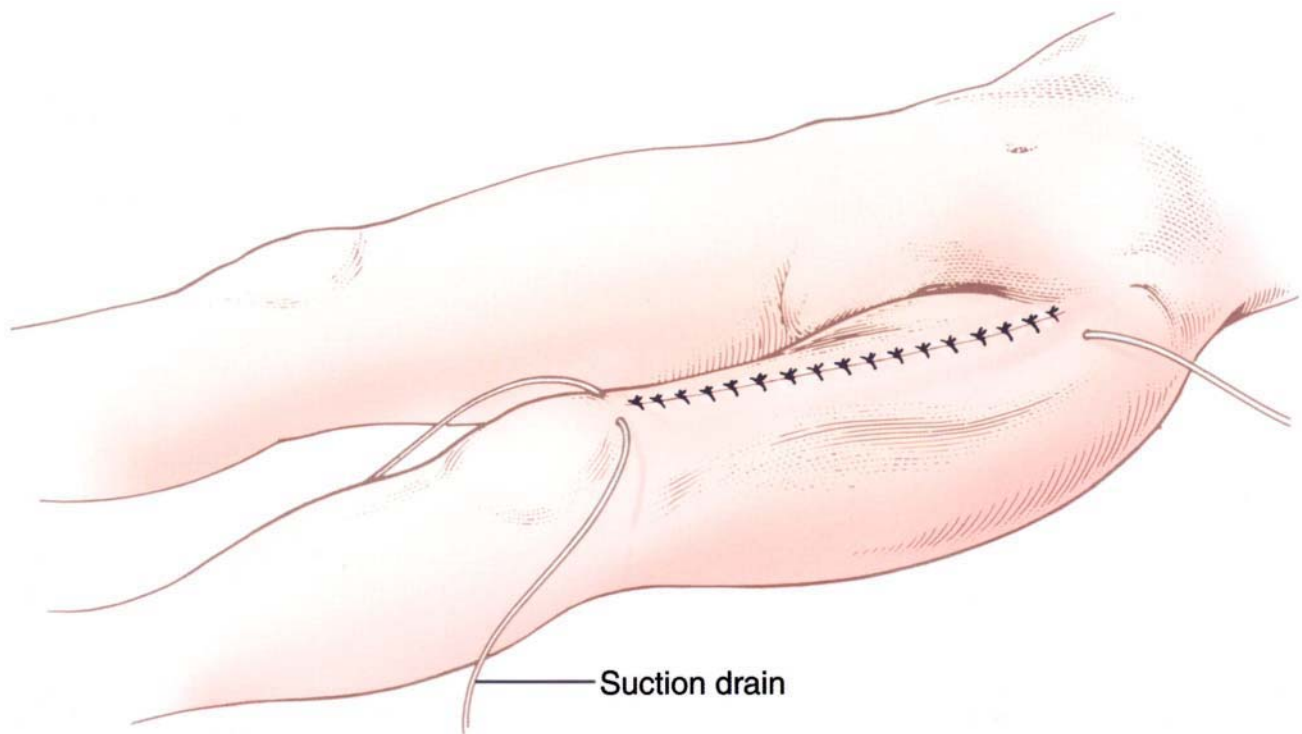


Figure 14.12 Closure. Suction catheters are placed beneath the skin flaps and the subcutaneous tissue is approximated with interrupted absorbable sutures. The skin is closed. No immobilization using plaster is required and the incision is merely covered with povidone iodine ointment and a loose dry sterile dressing. The patient may begin ambulation when the suction catheters have been removed and edema of the leg has resolved. Because lymphatics along the superficial femoral artery and within the buttock remain intact, prolonged swelling is not usually a problem. Also, because muscles have been removed from origin to insertion, serous drainage from transected muscle bundles does not occur in large amounts. The patient ambulates initially with crutches and a touchdown gait.

DISCUSSION

Today, preoperative induction chemotherapy and/or radiation therapy permits a safe limb-sparing resection of approximately 95% of all soft-tissue sarcomas of the anterior thigh. The authors prefer preoperative induction chemotherapy for most high-grade soft-tissue sarcomas of the anterior thigh. We utilize postoperative radiation therapy only if there is less than 90% tumor necrosis or for a close surgical margin.

The major anatomic considerations in treating tumors of the anterior thigh are the femoral vessels and the relationship of the tumor to the underlying femur. The superficial femoral artery must be evaluated by biplane angiography and, if necessary, resection and a vascular graft are performed. It is important to note that the vastus intermedius protects the underlying femur from most tumors of the other anterior muscles. Arising from the entire diaphyseal surface of the femur and from the linea aspera, the vastus intermedius is interposed between the femoral shaft and the remaining quadriceps muscles. If a tumor arises within the intermedius muscle, an amputation can still be avoided by administering induction chemotherapy and/or radiation therapy, resecting the vastus intermedius, and utilizing high-speed burr to remove the outer 2–3 mm of the exposed femoral cortex. A cortical resection is never performed.

The main indications for amputation are large, fungating tumors, especially of the proximal thigh and groin; extracompartmental extension into the adductor and/or hamstring compartments; intrapelvic extension below the inguinal ligament; or a combination of the above.

In general, most patients today are treated by partial muscle group resections of the quadriceps muscles, followed by radiation therapy. Induction chemotherapy or radiation therapy is performed in several centers. If a portion of the anterior thigh musculature remains, reconstruction is not required. If the entire anterior thigh musculature is removed, reconstruction is performed by centralizing the long head of the biceps femoris and the sartorius and gracilis muscles anteriorly along the anterior aspect of the thigh and suturing into the patellar tendon. This restores functional stability of the knee. In general, the results of this transfer are good, and active knee extension is restored. If radiation therapy is required, lymphedema is usually not a problem because the lymph nodes are not routinely resected. Lymph node involvement rarely occurs with soft-tissue sarcomas.

Today, the quadriceps compartment can generally be safely resected and reconstructed. Amputation is rarely required.

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Resection of the Posterior Compartment of the Thigh

Martin Malawer and Paul Sugarbaker

OVERVIEW

This chapter discusses the anatomic considerations, staging studies, techniques of biopsy and indications and contraindications to the treatment of posterior thigh sarcomas.

In general, the posterior thigh (hamstring musculature) is the least common of the three compartments of the thigh for sarcomas to arise within. There is great variation in the size of tumors that occur in the posterior thigh, and variation in the location from a proximal location near the ischium to a distal location involving the popliteal space.

The posterior thigh is a quiet surgical area with the most significant structure being the sciatic nerve. Almost all low-grade sarcomas can be resected safely. Most high-grade sarcomas can be resected by either a complete or partial muscle group resection. The sciatic nerve is rarely involved; even if resection is required, an amputation is not necessary.

Preoperative examination must evaluate the ischium, ischiorectal space, the retrogluteal area, and the popliteal space for tumor extension. The most useful imaging studies are CAT and MRI scans. Angiography is required only if the tumor extends distally into the popliteal space. Function following posterior thigh resection is almost normal. Knee flexion is maintained by the remaining sartorius, gracilis, and gastrocnemius muscles.

INTRODUCTION

The posterior compartment of the thigh is the least common of all of the thigh compartments for soft-tissue sarcomas to originate within. Approximately 15–20% of the soft-tissue sarcomas of the thigh arise within the posterior hamstring musculature. The posterior compartment consists of the semimembranosus, semitendinosus, and the long and the short heads of the biceps muscles. All of these muscles originate at the ischium and the linea aspera. The lateral hamstrings insert onto the fibular head whereas the medial hamstrings insert onto the medial and posteromedial aspect of the tibia and joint capsule. The most significant anatomic structure in the posterior compartment is the sciatic nerve that runs from the sciatic notch and passes just lateral to the ischium, then down the midposterior thigh, where it enters the popliteal space.

Classically, large tumors of the posterior thigh were treated by a hemipelvectomy. Today, most sarcomas of the posterior thigh can be resected by either a partial or total muscle group resection. The most crucial structures for evaluation are the sciatic nerve, popliteal space, and retrogluteal area. On rare occasions a compartmental resection may be performed with removal of the sciatic nerve. This allows for a functional extremity requiring only an ankle–foot orthosis (AFO).

ANATOMIC CONSIDERATIONS

The posterior thigh compartment consists of the semimembranosus and semitendinosus muscles and the long and short heads of the biceps. These originate from the ischium and along the linea aspera. There is no major artery that is involved with this compartment. The sciatic nerve is the most significant structure and passes into the compartment from lateral to the ischium and divides the medial and lateral hamstrings. The nerve is surrounded by a large layer of fibro-fatty tissue. A thick sheath surrounds the nerve, acting as a barrier to direct tumor extension. Often tumors arise within one of the individual muscles of the posterior thigh or between the muscles. In most cases the sciatic nerve is displaced around an adjacent muscle.

UNIQUE ANATOMIC CONSIDERATIONS

The specific anatomic sites to be evaluated prior to a limb-sparing resection are the following:

1. *Retrogluteal area* (beneath the gluteus maximus muscle). Tumors of the hamstring muscles may involve proximal extension into the retrogluteal area and adjacent to the ischium. Extension into this compartment must be taken into consideration at the time of resection.
2. *Ischium*. The ischium is the site of proximal origin of all of the hamstring muscles. Tumors that extend close to the ischium may extend into the ischiorectal space or to the inferior pubic ramus as well as the ischium.
3. *Sciatic nerve*. The sciatic nerve runs from the sciatic notch through the midline of the thigh posteriorly to the popliteal space where it divides into the peroneal and tibial nerves. The relationship of the sciatic nerve to a sarcoma arising in the posterior compartment is extremely important to determine. True sciatic nerve involvement is rare. Most often the sciatic nerve is displaced but not directly invaded by tumor. Rarely are there primary sarcomas arising from the nerve itself.
4. *Popliteal space*. The popliteal space is the distal end of the posterior compartment. It is made up of the short head and long head of the biceps on the lateral aspect, and the semimembranosus on the medial aspect. The popliteal artery and vein enter through the adductor hiatus on the medial side; therefore, tumors that arise in the posterior thigh that extend into the popliteal space may easily involve the popliteal artery and vein. It is essential to evaluate these structures prior to surgery.

STAGING STUDIES

CAT Scan and MRI

CAT scan and MRI evaluation are excellent in determining the muscle involved by a sarcoma and the relationship of the adjacent sciatic nerve to the tumor (Figure 15.1).

Bone Scan

Bone scan may determine involvement of the underlying femur, linea aspera, or ischium. Tumors that involve the linea aspera may become extracompartmental by passing into the anterior or medial compartments of the thigh.

Biplane Angiograms

Angiography is required to determine the relationship of the popliteal artery and vein to tumors extending to the distal portion of the posterior thigh (Figure 15.2A). Most often these vessels are displaced. Tumor extension into the popliteal space makes resection more difficult but not impossible.

Biopsy

Multiple core needle biopsies of the tumor mass are preferred. The puncture site should be near the midline

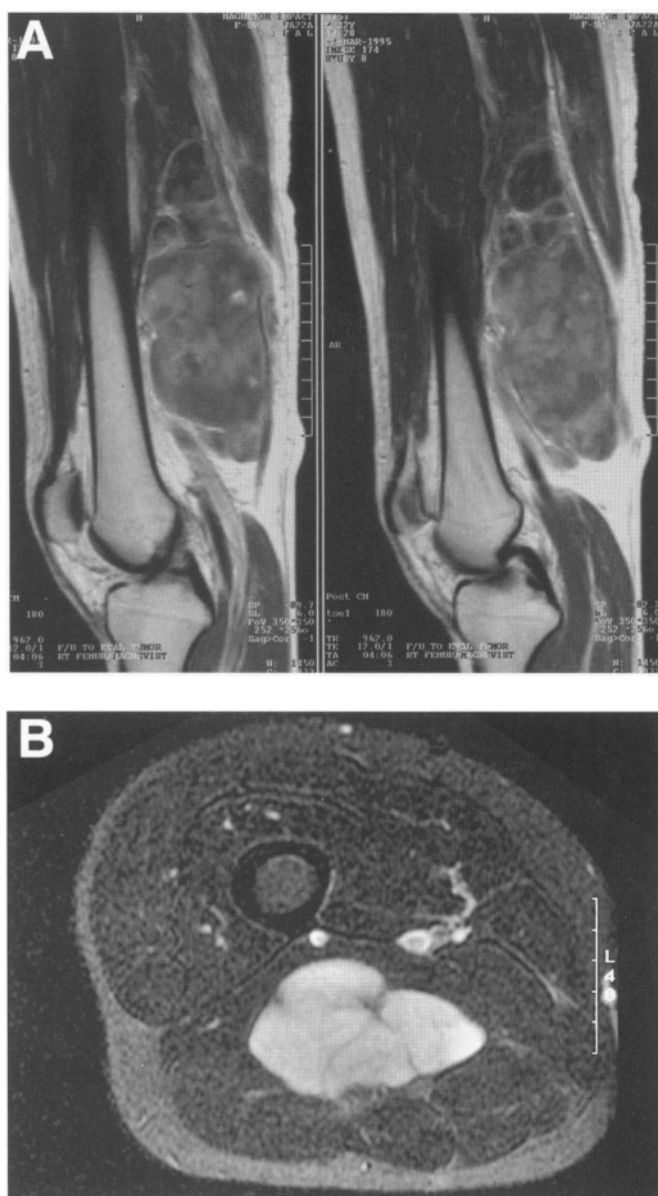


Figure 15.1 MRI scans for evaluation of posterior thigh compartment. (A) Sagittal T1 weighted image of a moderately sized posterior thigh sarcoma. Tumors of the posterior thigh often displace but rarely involve the adjacent sciatic nerve. The sciatic nerve can rarely be visualized well on an MRI scan. It is important to note that this tumor does not extend into the popliteal space as it approaches it. Angiography is utilized if tumor extends into the popliteal space. (B) Axial T2 weighted MRI scan of the same tumor that shows it arises between the medial and lateral hamstring muscles, not within the muscle itself. This is termed an extramuscular versus extracompartmental origin. The sciatic nerve cannot be well visualized and it is our policy to explore these lesions with the aim of resection and preservation of the nerve. Only if the nerve is encased by tumor is an amputation recommended. However, sciatic nerve resections with good postoperative extremity function have recently been reported.

of the posterior thigh with the needle directed toward the underlying muscle and tumor. This site is in the line of anticipated resection (Figure 15.2). The definitive incision extends from the ischium along the midline of the posterior thigh and then to the popliteal space.

INDICATIONS AND CONTRAINDICATIONS

Almost all low-grade sarcomas of the posterior thigh can be treated by partial or total resection of the involved muscle. Intramuscular or extramuscular tumors are treated by wide excision. If the tumor is extramuscular, but still remaining within the compartment, a partial muscle group resection is performed. High-grade sarcomas are treated by complete myomectomy of the muscle involved. Multiple muscles or the entire compartment can be resected in lieu of an amputation (Figure 15.3).

Contraindications for posterior compartment soft-tissue tumor resections include:

1. *Extension into ischiorectal space.* This makes the resection more difficult and may indicate the need for an amputation.
2. *Popliteal space involvement.* Tumors of the posterior thigh that extend distally may involve the popliteal space and thus the popliteal artery and vein, and the peroneal and posterior tibial nerves. In these cases, this space must be explored prior to resection.
3. *Sciatic nerve involvement.* Direct involvement of the sciatic nerve usually indicates the need for amputation but rarely occurs. If adequate margins cannot be obtained with preservation of the sciatic nerve, then the nerve must be resected. The functional result with the sciatic nerve resected is far superior to that of a hemipelvectomy. These patients require only an ankle-foot orthosis (AFO) (Figure 15.4).
4. *Femoral involvement.* If the underlying femur is involved by tumor as shown by CT scan or bone scan, partial resection of the linea aspera is required; otherwise, an amputation is recommended. A high-speed burr is utilized for resection of the outer 2 or 3 mm of the linea aspera.
5. *Ischial involvement.* Large posterior tumors may involve the ischium and extend into the ischiorectal space or proximally into the retrogluteal area. Proximal tumor extension may indicate the need for an amputation.

GUIDELINES OF SURGICAL TECHNIQUE

The surgical technique is summarized (Figures 15.5–15.13):

1. The incision extends from the ischium curving toward the midline, down the posterior thigh to the

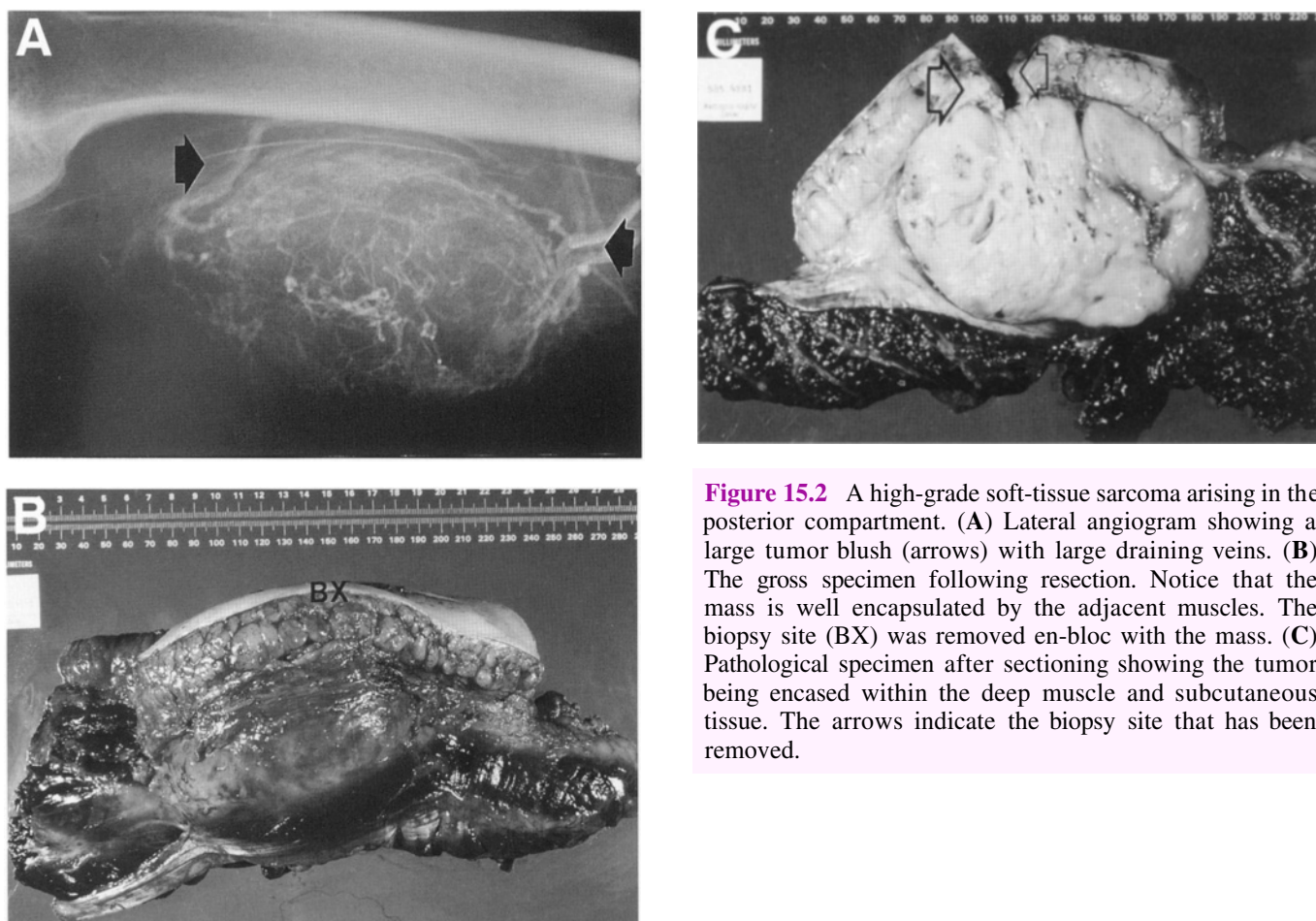


Figure 15.2 A high-grade soft-tissue sarcoma arising in the posterior compartment. (A) Lateral angiogram showing a large tumor blush (arrows) with large draining veins. (B) The gross specimen following resection. Notice that the mass is well encapsulated by the adjacent muscles. The biopsy site (BX) was removed en-bloc with the mass. (C) Pathological specimen after sectioning showing the tumor being encased within the deep muscle and subcutaneous tissue. The arrows indicate the biopsy site that has been removed.

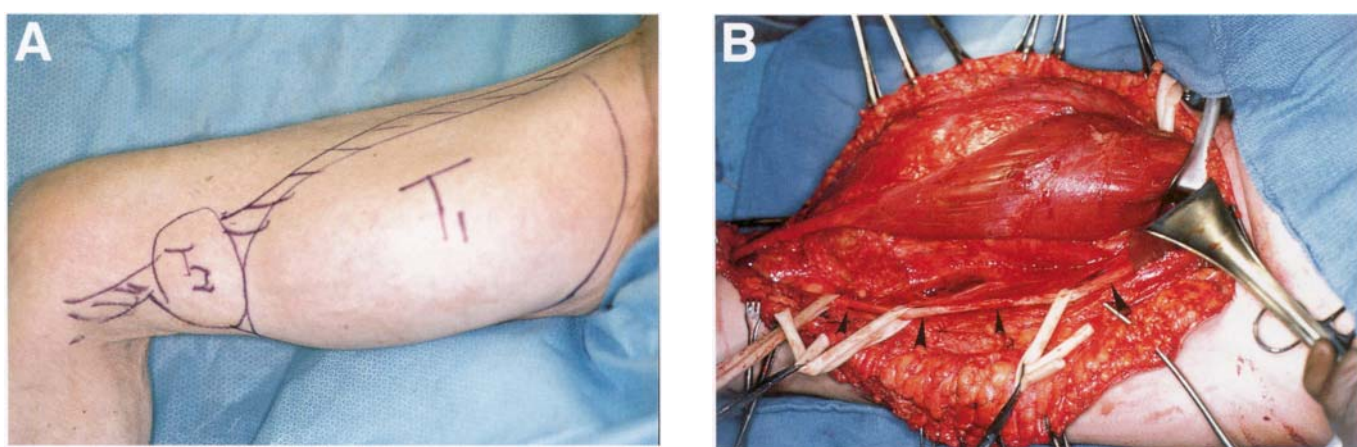


Figure 15.3 Clinical and intraoperative photographs of a large hamstring tumor arising in the hamstrings. (A) Clinical photograph prior to incision showing the large size of the tumor involving the hamstrings with displacement of the adductor muscles. T1 and T2 represent two large palpable masses. The cross-hashed area indicates the palpable pulse and the sartorial canal. Similar to adductor group resections, large posterior hamstring muscle tumors may invade adjacent structures and should involve exploration of the superficial femoral artery and popliteal space prior to resection. This can often be determined by the preoperative MRI (see above) and an angiogram. (B) Intraoperative photograph demonstrating that the entire posterior compartment is being elevated, showing the tumor is located in the medial and lateral hamstrings. Note the sciatic nerve has been dissected completely free and appears not to be involved (arrows). The sciatic nerve must be exposed from the sciatic notch to the popliteal space. Functional results after posterior compartmental resection are excellent with minimal gait disturbance.

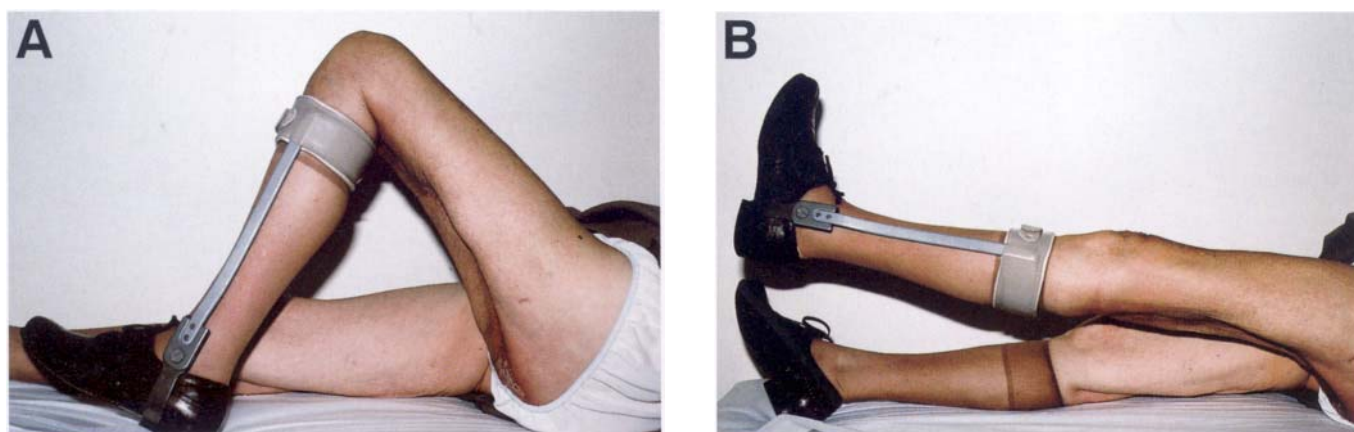


Figure 15.4 (A and B) Clinical photographs of a patient who has undergone resection of the posterior thigh compartment along with the sciatic nerve. The main functional need is an AFO (ankle-foot orthosis) to stabilize the foot in gait. Knee extension is normal and knee flexion is adequate due to the gastrocnemius heads, sartorius muscle, and gracilis muscle. In addition, if the tumor is resected distal to the pedicle of the biceps, and if the biceps can be preserved, then knee flexion is even improved.

level of the popliteal space, and then across the popliteal space in an S shape (from medial to lateral). It then passes to the fibular head. This incision permits exposure of the popliteal space, the sciatic nerve and both medial and lateral hamstrings, as well as their origin from the ischium (Figures 15.5–15.7).

2. Resection consists of releasing the origin of the hamstring muscles from the ischium and exploring the retrogluteal area at the time of resection for proximal tumors, as well as the ischiorectal space, to make

sure that there is no tumor extension (Figures 15.8–15.10).

3. Popliteal space exploration is required if the tumor is distal in the posterior thigh. The popliteal artery and vein as well as the sciatic nerve are explored and retracted.
4. The involved muscles are released from either the medial aspect of the knee or the fibula and the entire muscle group can then be resected from the linea aspera (Figures 15.11–15.13).

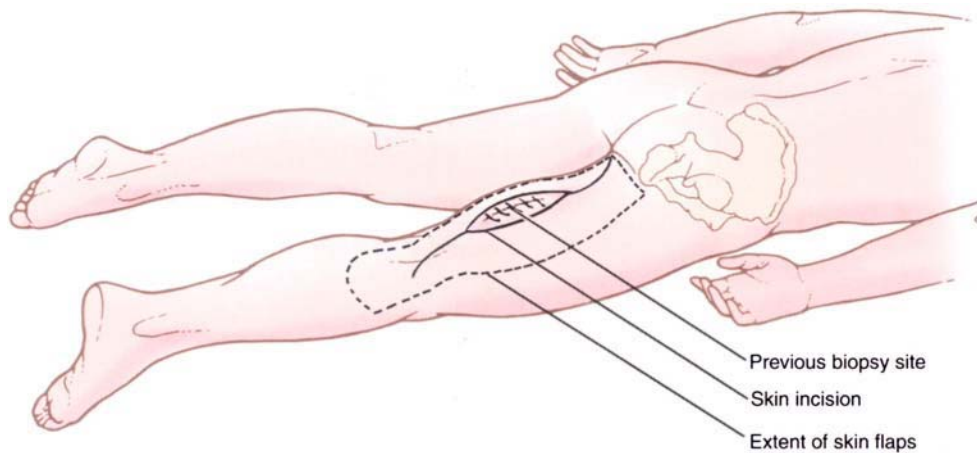


Figure 15.5 Incision and skin flaps. The patient is placed in the prone position. An ellipse of skin is outlined so that there is a 2 cm margin of skin around the old biopsy site. The extents of the skin flaps are dissected, care being taken to taper the flaps, as one encounters the lateral margins of the dissection. It is helpful to mark on the skin the extent of the dissection of the skin flaps so that one does not inadvertently exceed this during the dissection. The medial extent of the dissection is the gracilis muscle, and the lateral extent is the iliotibial tract.

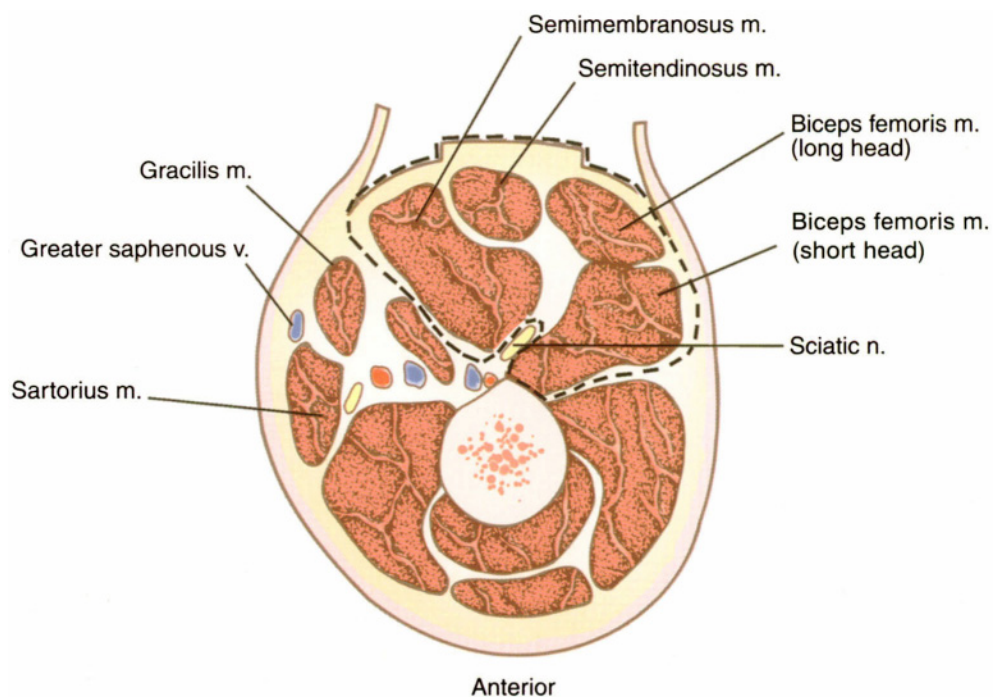


Figure 15.6 Cross-section of the mid-thigh. The proximity of the sciatic nerve to large sarcomas within the posterior compartment is clearly indicated by this diagram.

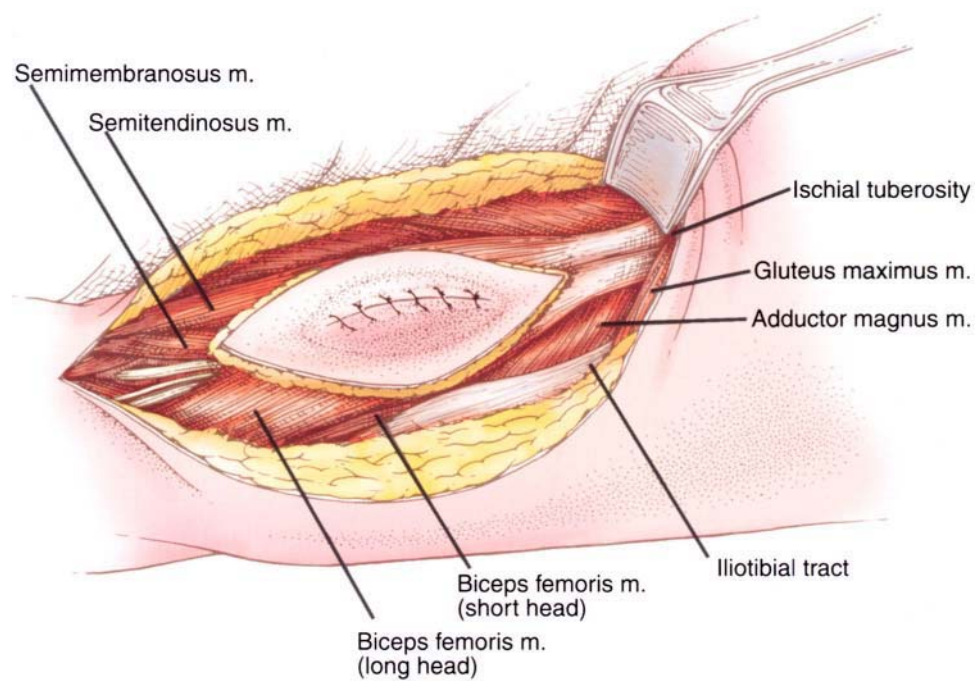


Figure 15.7 Creation of the skin flaps. The medial (semitendinosus and semimembranosus muscles) and lateral (biceps femoris long head and short head) muscles are exposed.

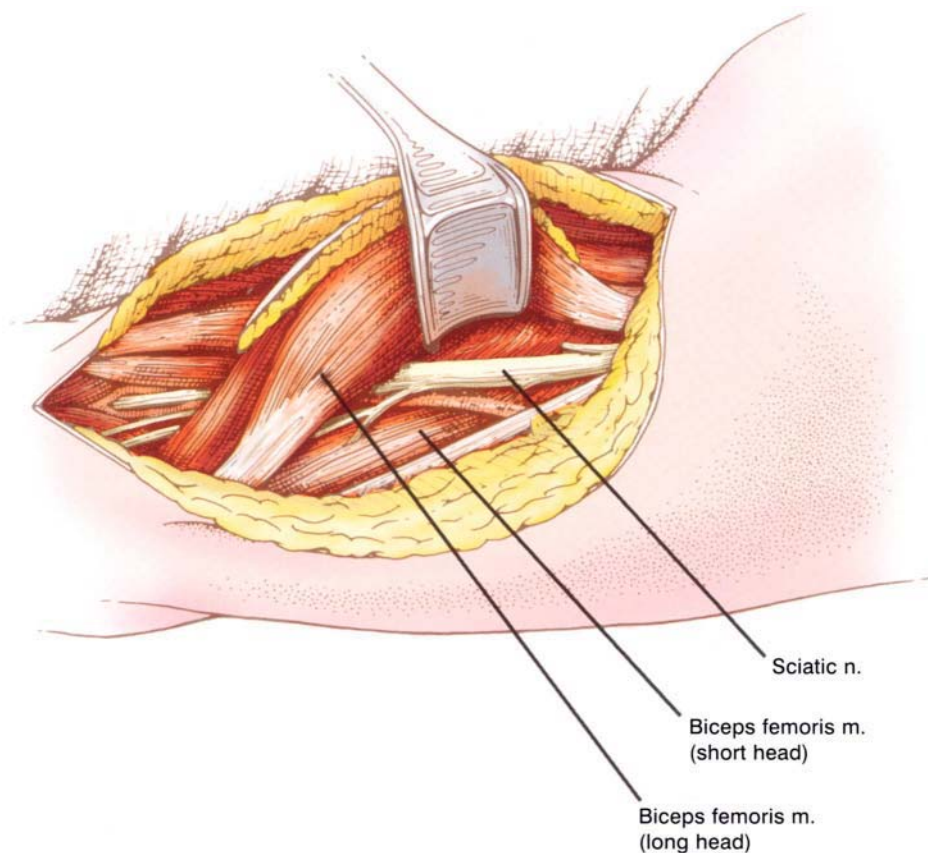


Figure 15.8 Defining the muscles of the posterior compartment. The extent of the dissection is determined by the location of the sarcoma, but resection generally involves the long head of the biceps femoris, semimembranosus, and semitendinosus. It is possible for a portion of the lateral quadriceps mechanism to be included with the specimen. Likewise, one or more muscle bundles of the adductor muscle group may be included with the muscle group, if this will afford a more generous margin. The three muscles mentioned are superficial to the sciatic nerve, and their origin is from the ischial tuberosity. A tumor-free margin of resection depends on a tumor-free plane superficial to the posterior limits of this compartment. It is clear that the next adjacent structure is the sciatic nerve itself.

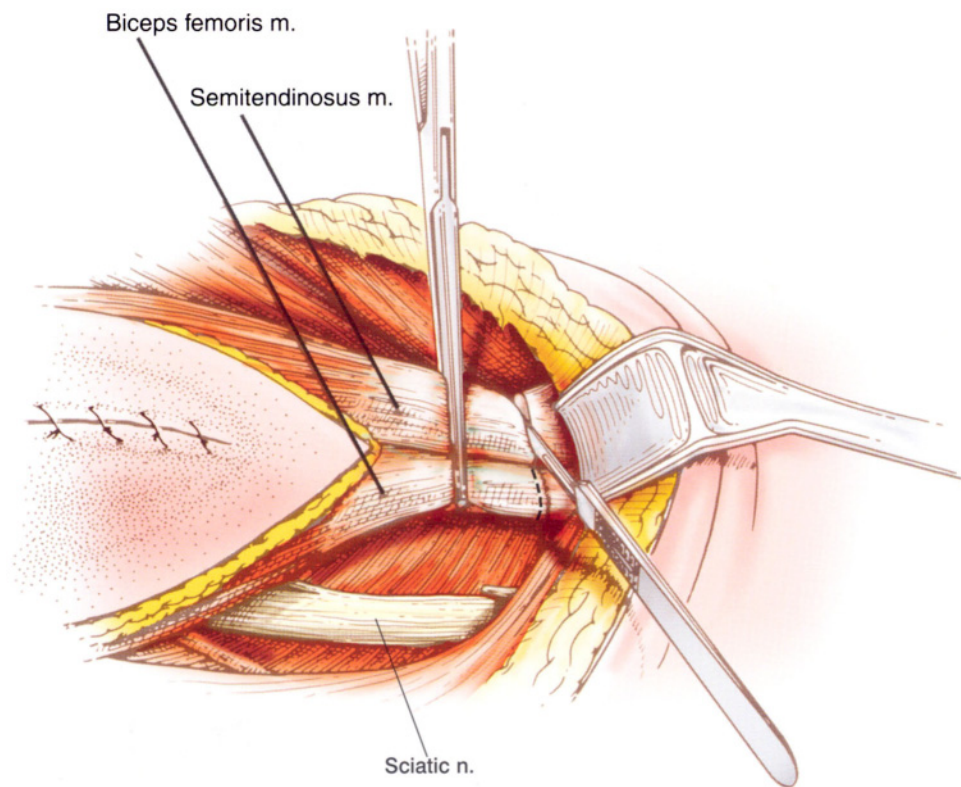


Figure 15.9 Transection of muscle origins. Dissection begins by exposing the ischial tuberosity. It is easily identified on the skin surface. The hamstring muscles are released at their origin from the ischial tuberosity.

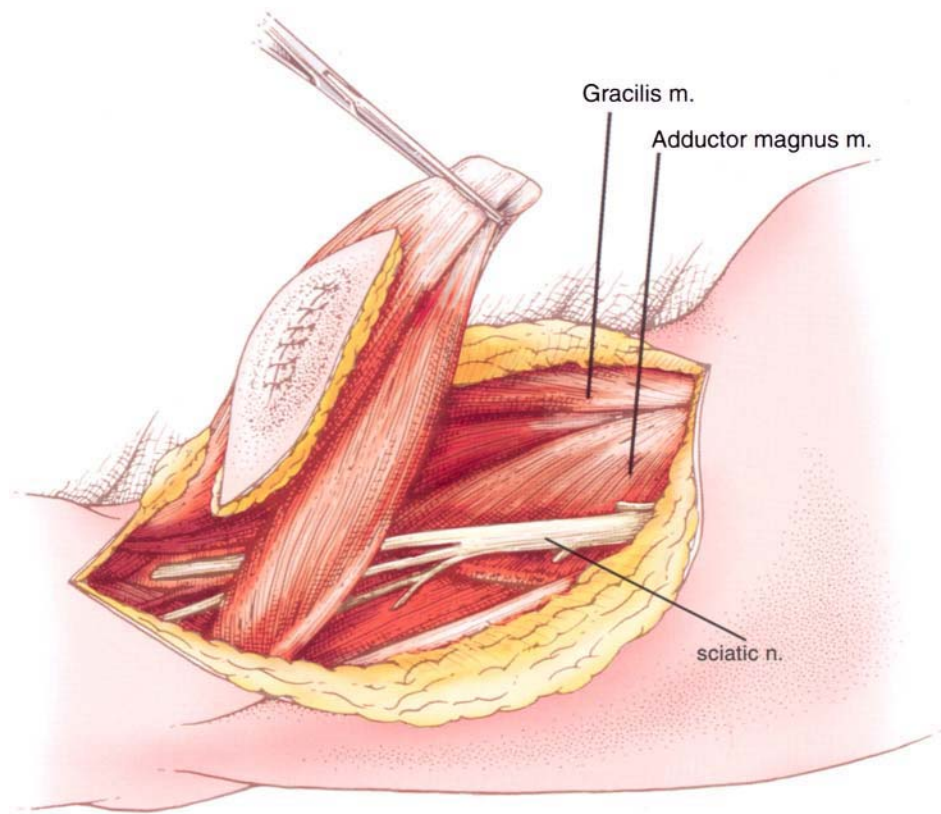


Figure 15.10 Dissection of the muscle group from proximal to distal aspects. The muscle groups are secured with a clamp, and strong traction is placed on the muscle group. Blood vessels and nerves that enter the hamstring muscle are ligated and divided. By means of blunt and sharp dissection, the sciatic nerve, the short head of the biceps laterally, and the adductor muscles medially are elevated from the base of the dissection.

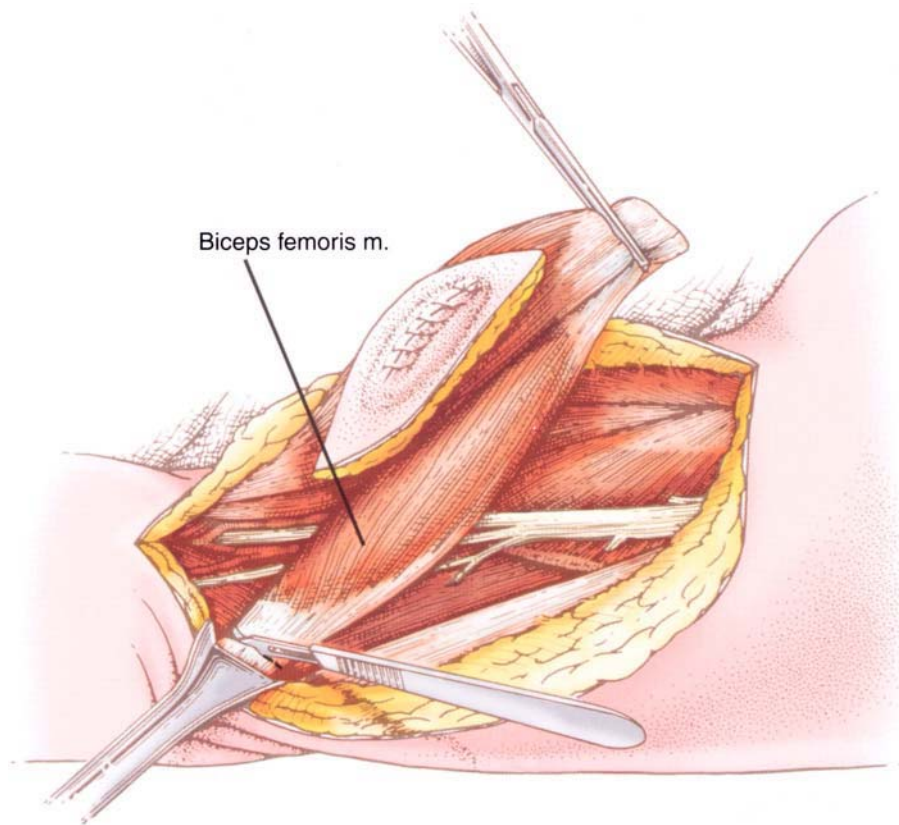


Figure 15.11 Transection of muscle insertions laterally. The long head of the biceps femoris muscle is transected through its tendinous portion on the lateral aspect of the thigh. One must take care to avoid injury to the common peroneal nerve.

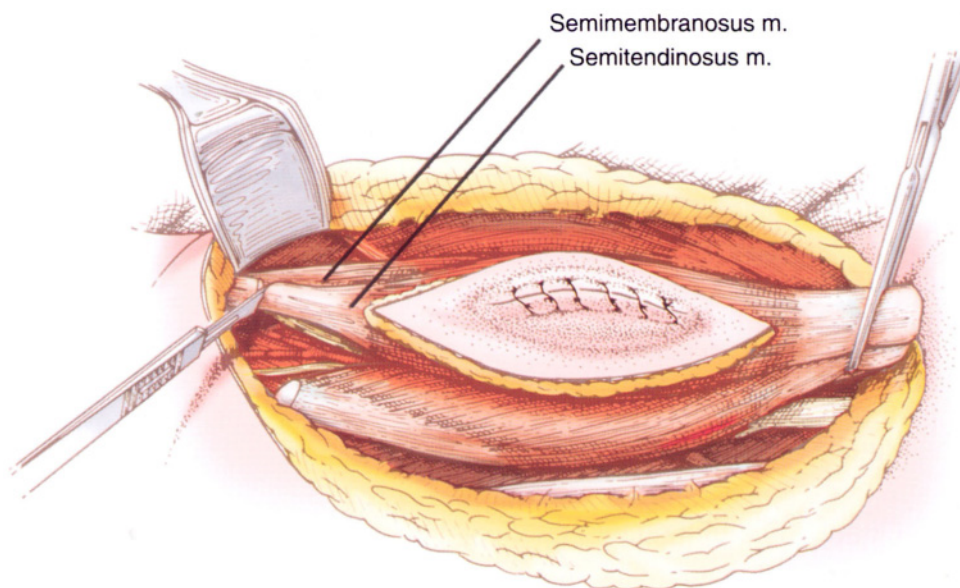


Figure 15.12 Transection of muscle insertions medially. The insertions of the semimembranosus muscle and semitendinosus are divided through their tendinous portions medially. The medial head of the gastrocnemius muscle is exposed.

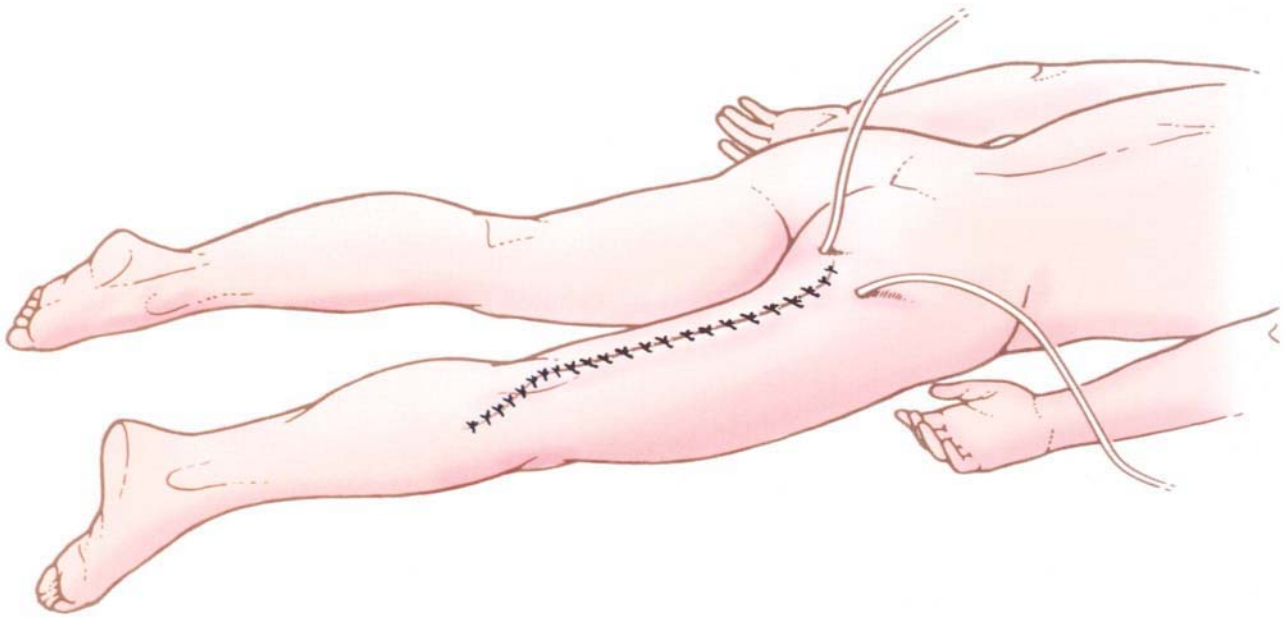


Figure 15.13 Closure. The superficial fascia and skin are meticulously closed. Generous suction drainage is achieved through suction drains. Care should be taken not to make the skin exit sites for the suction drains through the skin flaps; rather, these should be just above the gluteal crease.

DISCUSSION

Tumors of the posterior thigh are almost always resectable. Sarcomas arising in this area are often small, though they may become extremely large. Fortunately, the sciatic nerve is often displaced around an adjacent muscle or the pseudocapsule and can usually be preserved. Direct sciatic nerve involvement is rare.

Induction chemotherapy is recommended for high-grade sarcomas prior to resection attempt. If the tumor is confined to one muscle belly, a true myomectomy can be performed. If the tumor is extramuscular and involves two or three muscle bellies, all involved muscles can be resected with good margins. The sciatic nerve sheath should be exposed in the portion that is closest to the tumor to determine if there is any tumor involvement of the sheath. A complete sciatic nerve sheath resection can be performed. Alternatively, the sciatic nerve itself may be resected without having to proceed to an amputation. The function following a sciatic nerve removal is extremely good, with knee flexion being supplied by the remaining sartorius and gracilis muscles, as well as the gastrocnemius muscles.

The sciatic nerve is the most significant structure in the posterior compartment. There are no imaging studies that can reliably demonstrate the relationship of the tumor to the sciatic nerve. Both the MRI and CAT may be useful, although the deciding factor to proceed with a resection or amputation can sometimes only be made at the time of exploration of the posterior thigh. During exploration it is possible to determine the relationship of the sciatic nerve to the tumor. It is rare for the sciatic nerve to be directly infiltrated by tumor.

The relative contraindications to a posterior thigh resection are usually a combination of factors:

ischiorectal extension, popliteal space extension, possible sciatic nerve involvement, and/or femur involvement. Any one of these anatomic restraints can be incorporated into an adequate resection, but a combination usually indicates that an amputation is warranted. The level of amputation is above the pelvis; that is, a hemipelvectomy. Fortunately, today, most posterior thigh sarcomas can be treated by induction chemotherapy followed by resection and/or radiation therapy postoperatively. Function following a posterior thigh resection is usually very acceptable to the patient.

Imaging studies are very reliable for most tumors of the posterior thigh (Figure 15.2). The most significant structure is the sciatic nerve that can best be visualized with a CAT or MRI. Often the posterior thigh should be explored prior to proceeding with an amputation in order to determine the degree of involvement of the sciatic nerve. Hemipelvectomy is usually required if there is large extracompartmental extension either into the anterior thigh or the medial compartment. Other sites of extracompartmental extension include the ischiorectal space and the retrogluteal area.

The posterior compartment is an extremely quiet area for tumors, with few restrictions to resectability. The surgical technique essentially removes the entire hamstring musculature from its origin on the ischium to its insertion onto the fibular head and medial aspect of the knee joint. The sciatic nerve is usually preserved. The function following a posterior thigh resection is usually excellent with good knee flexion being maintained by the remaining musculature of the sartorius, gracilis, and gastrocnemius muscles. If the sciatic nerve has to be removed, knee flexion is still possible and only an AFO is required.

Resections in the Popliteal Fossa and the Posterior Compartments of the Leg

Jacob Bickels and Martin Malawer

OVERVIEW

Soft-tissue tumors of the popliteal fossa and the posterior compartments of the leg are relatively uncommon. Patients with such tumors formerly were treated with amputations; however, better understanding of tumor biology and advances in chemotherapy and radiation therapy now allow the performance of limb-sparing procedures in the majority of these cases. Most of these tumors are large and are in close proximity to the neurovascular bundle at presentation; therefore, careful preoperative evaluation and meticulous surgical technique are essential. The utilitarian approach enables wide and safe exposure of the popliteal fossa, superficial and deep posterior compartments of the leg, and the posterior aspect of the distal femur.

INTRODUCTION

Soft-tissue sarcomas and metastatic tumors of the popliteal fossa and posterior compartments of the leg have traditionally been treated with above-knee amputation. The major considerations governing the decision to amputate were the proximity to the neurovascular bundle and extent of soft-tissue involvement and resection. In addition, poor wound healing was expected as the result of the extensive resection, compromised blood supply to the surgical site, and the frequent need to administer adjuvant radiation therapy. Better understanding of the biological behavior of these tumors, the availability of effective chemotherapeutic agents, the administration of intra-arterial chemotherapy, and techniques of isolated limb perfusion now allow the performance of limb-sparing procedures in the majority of these cases.

This chapter describes the utilitarian approach to the popliteal fossa and posterior compartments of the leg, a technique that allows wide exposure and safe resection of tumors in these anatomic sites. This approach can also be used for resection of intracapsular lesions of the knee joint or for intralesional resection of benign, benign-aggressive, and low-grade sarcomas of the posterior aspect of the distal femur (Figures 16.1–16.5).

ANATOMIC CONSIDERATIONS

The utilitarian approach to the popliteal fossa and posterior leg involves structures that, if damaged, can produce a permanent, significant disability. Therefore, thorough knowledge of the anatomy of the popliteal space and leg is mandatory. The popliteal space is diamond-shaped; on its superior aspect it is bounded by the semimembranosus and semitendinosus muscles medially and by the biceps femoris muscle laterally. Its inferior boundaries are the two heads of the gastrocnemius muscle. The roof of the fossa is the thin popliteal fascia; the floor is the posterior aspect of the distal end of the femur, the posterior capsule of the joint, and the popliteus muscle, which overlies the proximal tibia (Figure 16.6).

The tibial nerve enters the popliteal fossa lateral to the popliteal artery and approximately in the middle of the fossa, it crosses the artery to its medial aspect and remains at that location. The common peroneal nerve slopes down the superolateral border of the popliteal fossa toward the medial aspect and along the biceps femoris tendon, where it enters a tunnel within the substance of the peroneus longus muscle.

The popliteal artery enters the popliteal space from its medial aspect through the adductor hiatus and lies directly behind the posterior capsule of the knee joint. It runs obliquely through the fossa and branches into

two superior, single middle, and two inferior genicular arteries. The inferior genicular vessels pull the popliteal artery toward the joint capsule and usually have to be ligated in order to allow mobilization of the popliteal vessels to either side of the popliteal fossa. After exiting the popliteal fossa the popliteal artery divides into its terminal branches: the anterior tibial, posterior tibial, and peroneal arteries. The popliteal vein lies between the tibial nerve and the popliteal artery (Figures 16.7 and 16.8). The short saphenous vein pierces the popliteal fascia to join the popliteal vein within the fossa.

It is traditionally taught that the short saphenous vein and the medial sural cutaneous nerve are key anatomic structures in any popliteal dissection. Knowing the location of these two structures makes it easier to find the tibial nerve, which is the most superficial structure within the popliteal fossa (the popliteal vessels lie below the nerve). Tumors of the popliteal fossa and the proximal aspect of calf commonly displace the anatomic landmarks above and below the popliteal fascia, making the above-mentioned maneuver impractical. In order to locate the components of the neurovascular bundle, it is necessary to expose regions that are proximal and distal to the popliteal fossa, identify the major nerves and vessels, and follow them to the popliteal fossa. That surgical concept is used whenever a tumor creates distortion of the normal anatomic planes. Specifically, the sciatic nerve is tracked between the medial and lateral hamstrings, and the popliteal vessels are tracked between the two heads of the gastrocnemius muscle. Occasionally, it is necessary to detach the origin of the medial gastrocnemius muscle in order to achieve a wider exposure.

The muscles of the leg are enclosed within fascial layers that define four distinct compartments: anterior, lateral, superficial posterior (soleus and gastrocnemius muscles), and deep posterior (deep flexors, tibial nerve, posterior tibial and peroneal arteries and nerves). Tumors of the popliteal space and the superficial posterior compartment can usually be resected with marginal to wide margins. However, tumors of the deep posterior compartment are usually associated with extensive involvement of the neurovascular bundle and, therefore, necessitate amputation. Fortunately, most soft-tissue tumors of the posterior leg are located within the superficial posterior compartment and are confined either to the gastrocnemius or the soleus muscles, and therefore can be resected.

PREOPERATIVE EVALUATION

As in any tumor resection, complete preoperative staging is mandatory. Computed tomography (CT) and

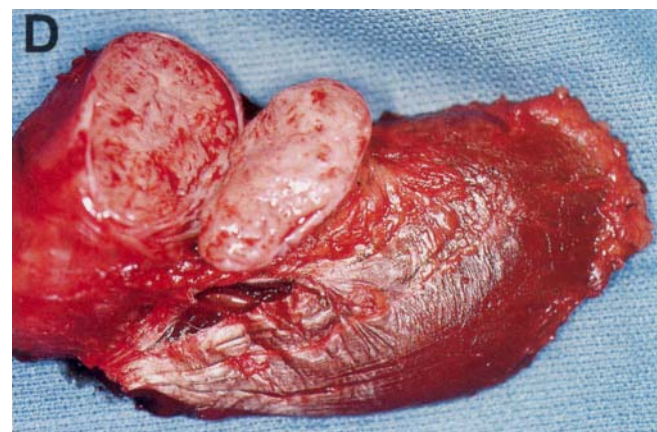
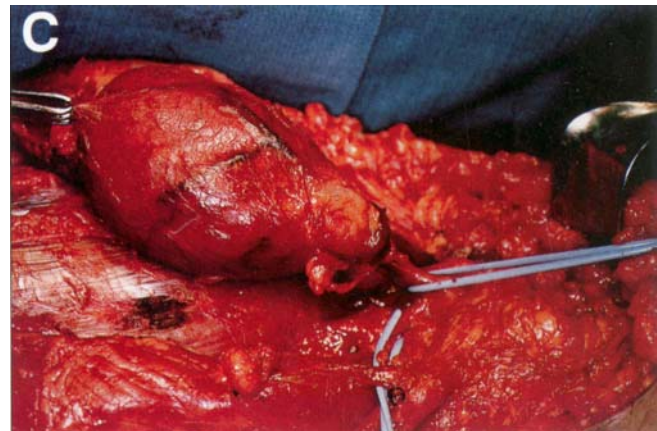
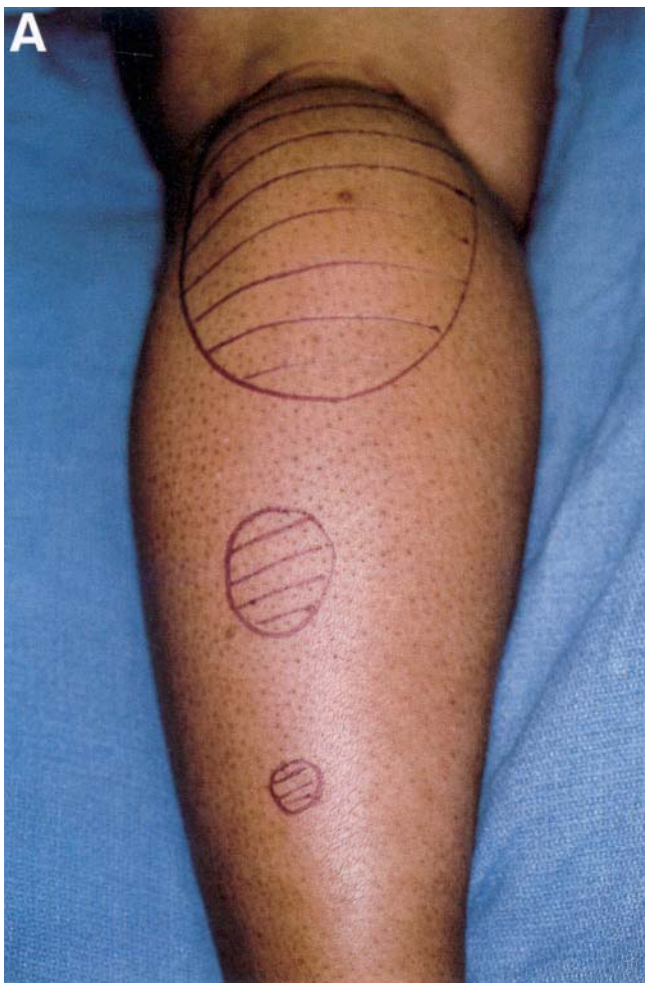


Figure 16.1 (A) A 40-year-old woman presented with a rapidly enlarging mass in her calf. Core-needle biopsy revealed a high-grade leiomyosarcoma. Additional skin marks represent skip nodules within the substance of the soleus muscle. (B) Sagittal T₁-weighted MRI of the superficial posterior compartment of the leg showing the tumor arising from the soleus muscle. (C) The posterior leg was approached using the posterior utilitarian incision. The soleus muscle (tumor) has been completely mobilized. The primary pedicle (vessel loop) is now ligated and transected. (D) Surgical specimen. The tumor was resected en-bloc with the underlying muscle.

magnetic resonance imaging (MRI) define the size of the tumor, the anatomic compartment to which it is confined, and its relation to the neurovascular bundle. The latter is best established with biplanar angiography, which also evaluates tumor vascularity and may assist

in the estimation of response to neoadjuvant chemotherapy, if given. Angiography is also essential in order to rule out vascular anomalies, which are relatively common in the tibioperoneal trunk. Bone scans are generally not helpful; however, increased uptake in an



Figure 16.2 Intermediate-grade liposarcoma of the popliteal space (arrows). The lesion was approached through the popliteal component of the utilitarian incision, and marginal excision was performed. The patient was treated with adjuvant radiation therapy.

adjacent bone suggests tumor extension and direct involvement.

SURGICAL TECHNIQUE

The patient lies prone on a frame with the operated extremity slightly flexed. The utilitarian approach to the popliteal fossa and posterior leg involves a curvilinear incision (**Figure 16.9**). The proximal limb of the incision follows the semitendinosus tendon distally to the level of the joint. It is curved laterally across the posterior aspect of the joint for about 5 cm and then turned distally along the lateral aspect or midportion of the posterior leg, depending on the aspect of the leg in which the lesion is located. The incision is extended to the level of the Achilles tendon (**Figure 16.9**). All or part of the incision can be used for adequate exploration and resection.



Figure 16.3 (A) Coronal T2-weighted MRI and (B) CT of the superficial posterior compartment of the leg showing a high-grade spindle-cell sarcoma within the soleus muscle.

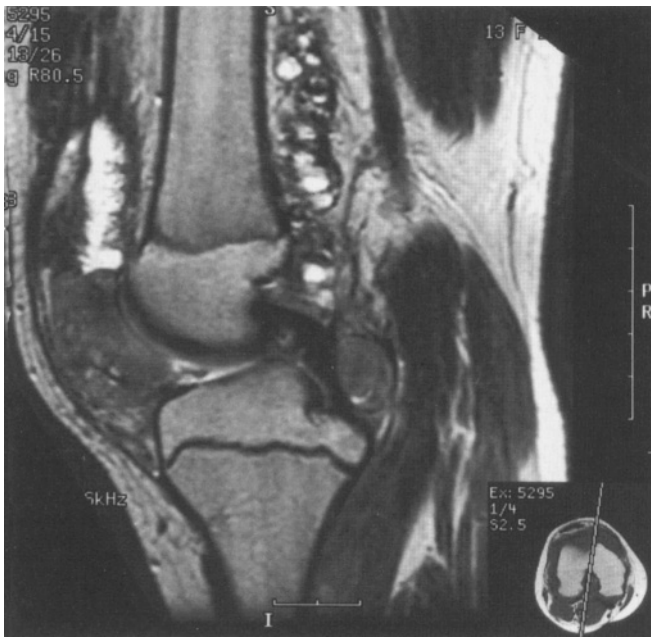


Figure 16.4 Pigmented villonodular synovitis of the knee joint in a 13-year-old patient. The patient underwent staged synovectomy (i.e. posterior synovectomy through the popliteal component of the utilitarian incision and anterior synovectomy a month later, once full range of motion was achieved) adjuvant radiation therapy was given.

The initial step of any resection around the popliteal fossa and posterior leg is exposure of the popliteal fossa and identification of the neurovascular bundle. This allows the surgical team to mobilize the vulnerable structures prior to resection. Skin flaps and subcutaneous tissues are raised and reflected. The popliteal fascia, which is very thin and friable, serves as a landmark because of its close proximity to the neurovascular bundle. Identification of the popliteal fascia is crucial, because if the surgeon does not realize that the dissection is underneath the fascia and only a few millimeters of fatty tissue separate the blade from the neurovascular bundle, he may continue the dissection, assuming that he is still within the thick layer of popliteal fat, and may injure a component of the neurovascular bundle.

If posterior synovectomy or excision of a bone tumor from the posterior distal femur is planned, the neurovascular bundle is mobilized to one side and the joint capsule is opened using a longitudinal arthrotomy. The medial or lateral heads of the gastrocnemius muscles may be detached to facilitate exposure of the joint or the distal femur.

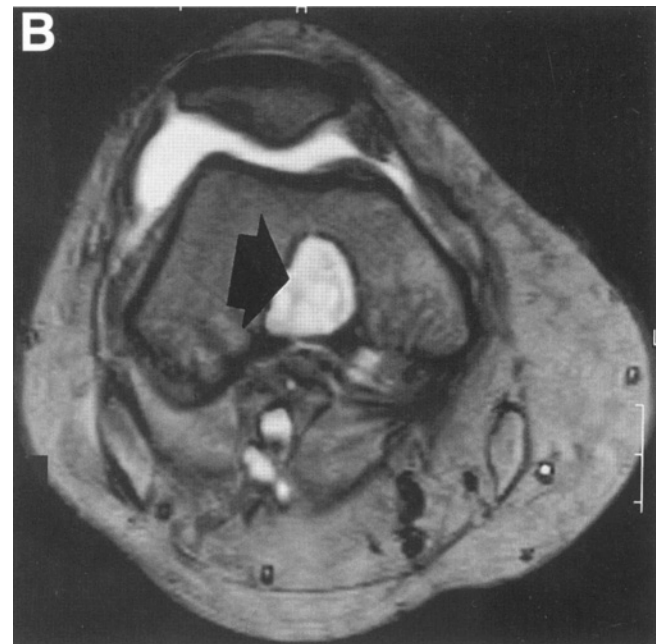
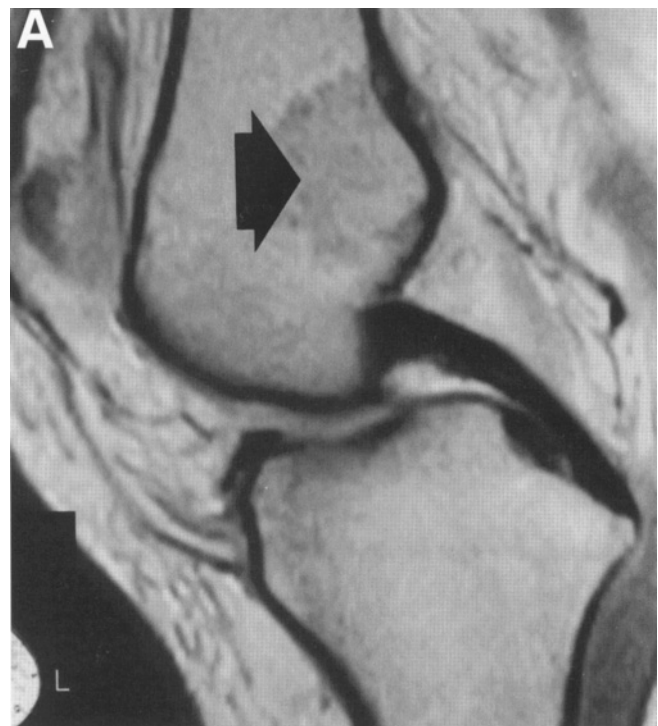


Figure 16.5 (A) Sagittal and (B) axial MRI of a low-grade chondrosarcoma (arrow) of the posterior aspect of the distal femoral metaphysis. The tumor was approached through the popliteal component of the utilitarian incision.

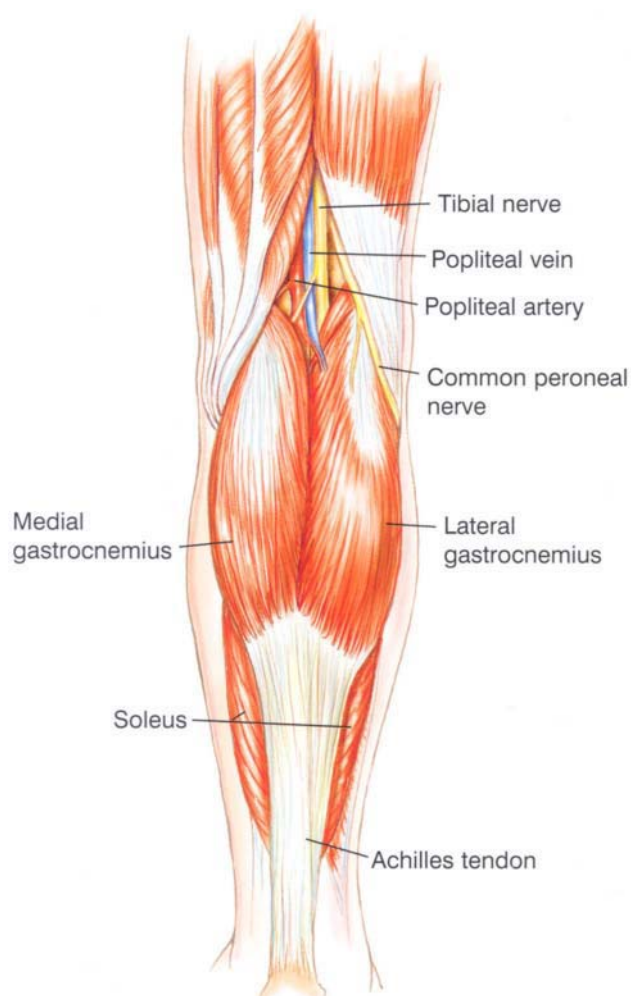


Figure 16.6 Anatomy of the popliteal fossa and the posterior compartments of the leg.

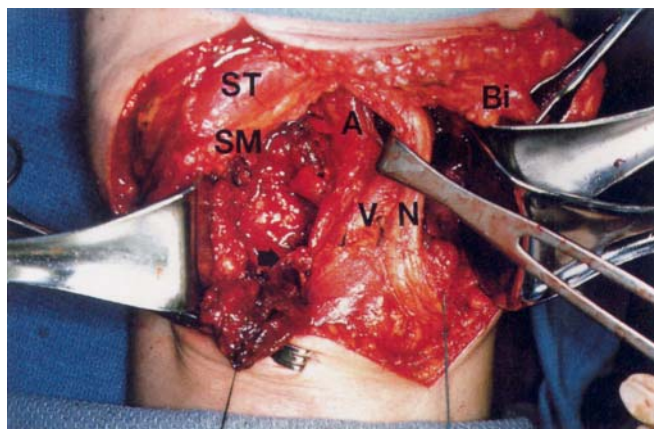


Figure 16.7 Wide exposure of the popliteal fossa. ST = semitendinosus muscle, SM = semimembranosus muscle, A = popliteal artery, V = popliteal vein, N = tibial nerve, Bi = biceps femoris tendon. Arrow points to the ligated inferior medial genicular artery.

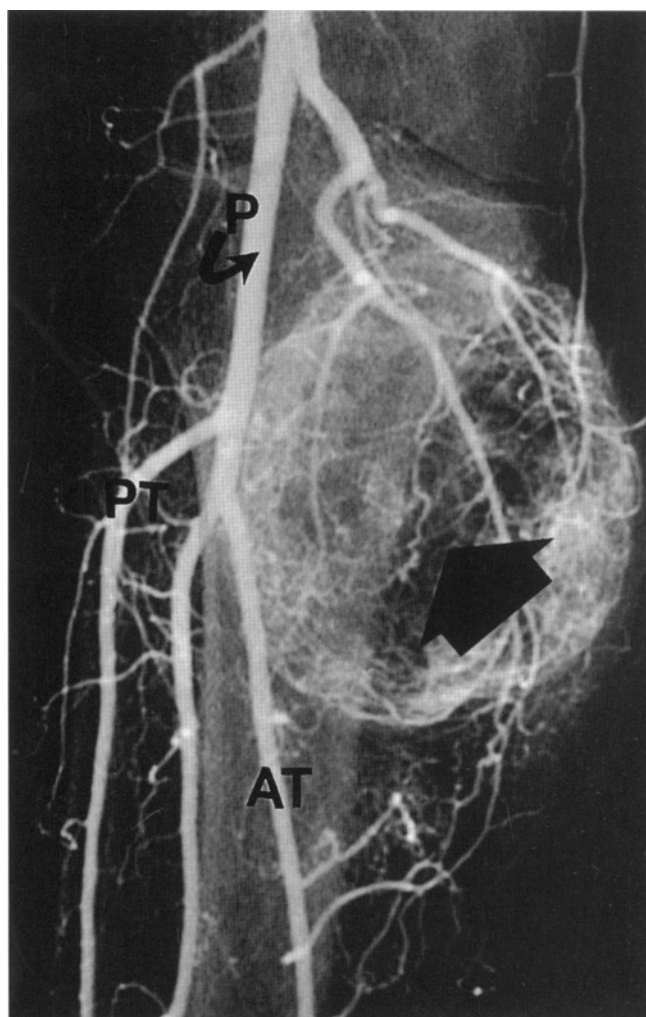


Figure 16.8 High-grade soft-tissue sarcoma of the medial gastrocnemius muscle. Popliteal angiogram shows a highly vascular lesion (arrow). The popliteal artery divides into its terminal branches (the anterior tibial, posterior tibial, and peroneal arteries). Following neoadjuvant chemotherapy, en-bloc resection of the medial gastrocnemius muscle and part of the soleus muscle was performed. (AT = anterior tibial, PT = posterior tibial, P = popliteal artery).

If resection around the posterior compartments of the leg is planned, the skin incision is extended distally along the planned resection site. A lateral incision is used if resection of the lateral gastrocnemius is planned. A midline posterior incision is used for resections of the medial gastrocnemius, soleus, and deep posterior compartment (Figure 16.9). Unlike the dissection in the popliteal space, the fascia is dissected with the subcutaneous tissues and large fasciocutaneous flaps are raised. Using electrocautery, the two heads of the

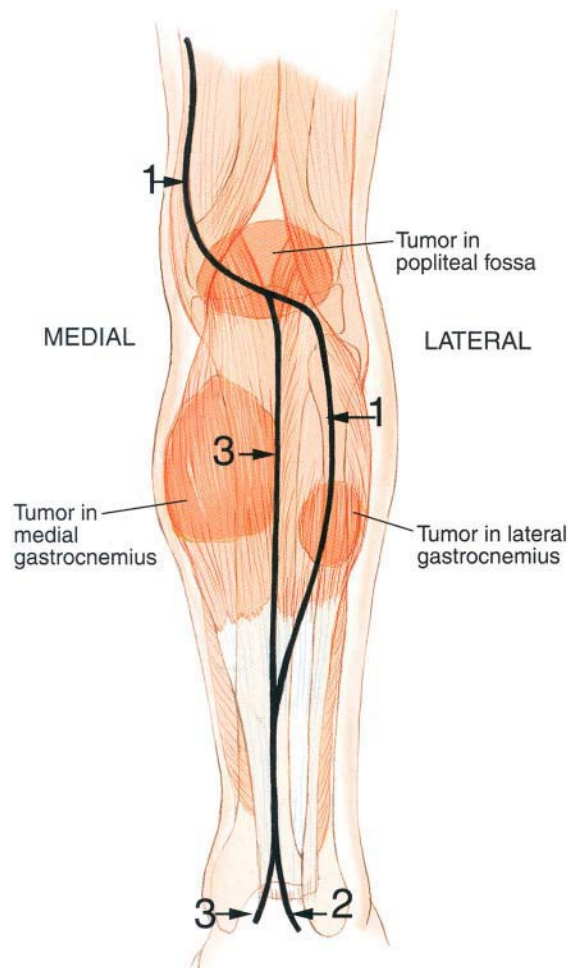


Figure 16.9 Utilitarian approach to the popliteal fossa and the posterior compartments of the leg. All or part of the incision can be used for adequate exploration and resection. Illustration shows tumors in the popliteal fossa, lateral gastrocnemius, and medial gastrocnemius muscles. A tumor in the popliteal fossa is approached through the popliteal component of the utilitarian incision (1–1). A tumor in the lateral gastrocnemius is approached through a lateral incision, and a tumor in the medial gastrocnemius or the soleus is approached through a midline incision (1–3–3).

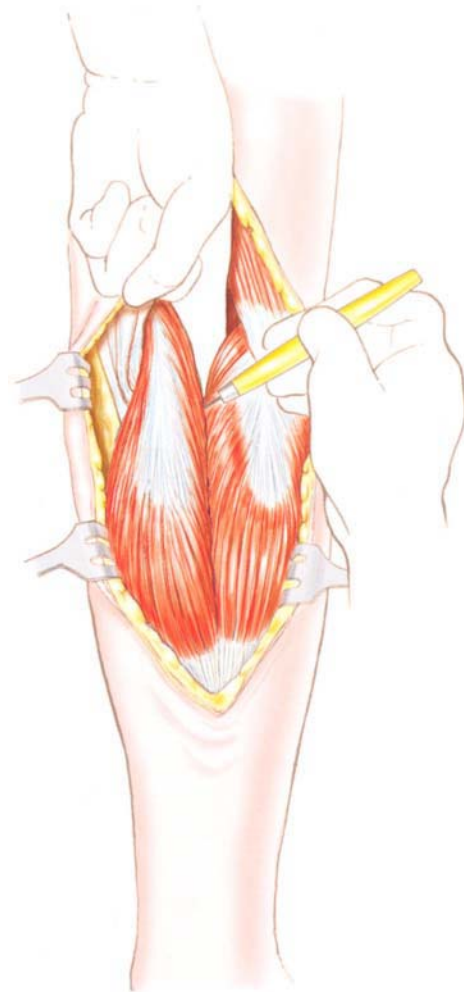


Figure 16.10 The interval between the medial and lateral gastrocnemius muscles is opened. The surgeon positions his finger between the gastrocnemius and soleus muscles to protect the neurovascular bundle that lies anterior to the soleus muscle, within the deep posterior compartment.

gastrocnemius flap are separated distally to the level of the Achilles tendon. The surgeon positions his finger between the gastrocnemius and the soleus muscles to protect the neurovascular bundle that lies anterior to the soleus muscle, within the deep posterior compartment (Figure 16.10). Radical excision of the medial or lateral heads of the gastrocnemius is achieved by reflection of the muscle, ligation of its main pedicle

(medial or lateral sural artery and vein, respectively), and transection of the femoral origin and insertion to the Achilles tendon.

Adequate exposure is essential for resection of the soleus. Proximally, it is achieved by reflection of the medial and lateral heads of the gastrocnemius. Partial or complete transection of the gastrocnemius femoral origin allows wide exposure of the proximal aspect of

the soleus, but imposes significant tension on the medial and lateral sural arteries, the main pedicles to medial and lateral gastrocnemius; it should therefore be practiced with caution. Distally, exposure is achieved by partial or, in rare cases, complete Achilles tenotomy (Figure 16.11).

By means of blunt dissection the soleus is separated from the transverse intermuscular septum, which outlines the deep posterior compartment. The soleus can then be detached from its tibial and fibular origins and calcaneal insertion. Appropriate plantar foot flexion can be preserved with just the medial gastrocnemius, lateral gastrocnemius, or soleus muscle. Any two of these structures may therefore be sacrificed without a significant impact on the range of motion around the foot. However, knee flexion can be significantly impaired under such circumstances. This is because the gastrocnemius muscle crosses the knee joint and the soleus muscle does not. Therefore, complete resection of the gastrocnemius will result in significant reduction in knee flexion capability, whereas resection of the soleus muscle and one of the heads of the gastrocnemius muscle will not.

If the joint capsule was opened, it must be closed prior to wound closure to avoid a potential synovial fistula. If part of the capsule was resected, and primary closure cannot be performed, one of the gastrocnemius heads or the popliteus muscle can be mobilized to seal the opening. The wound is closed over closed-suction drains. If extensive resection in the posterior leg was performed, a chest tube is added. To reduce tension on the suture lines, and avoid significant edema, the lower extremity is kept elevated in 15–20° of flexion in a posterior splint or a knee immobilizer for 3 days. Perioperative intravenous antibiotics are administered until the drainage tubes are removed. Postoperative mobilization with a knee immobilizer or posterior splint and weight-bearing as tolerated are required for about 3–4 weeks, depending on the extent of the soft-tissue resection and of satisfactory reconstruction. Active and active-assisted range of motion of the knee joint can then be introduced.

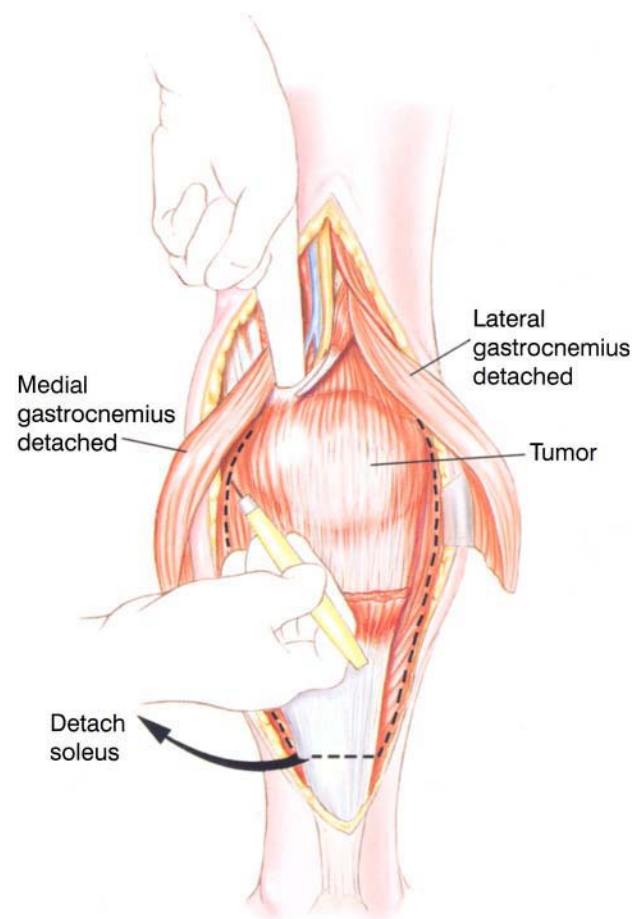


Figure 16.11 Exposure of the soleus muscle is achieved by reflection of the gastrocnemius heads and partial, or even complete, Achilles tenotomy, if necessary.

Section 3

Amputations

Forequarter Amputation

Martin Malawer and Paul Sugarbaker

OVERVIEW

Forequarter amputation entails surgical removal of the entire upper extremity, scapula, and clavicle. It was traditionally used for the treatment of high-grade bone sarcomas of the shoulder girdle, particularly osteosarcomas of the proximal humerus and scapula. Other indications included large and high-grade sarcomas of the axilla, brachial plexus and the suprascapular area of the shoulder.

As a result of advances in limb-sparing surgery for bony and soft-tissue sarcomas, forequarter amputation is rarely performed today. Only 5–10% of patients with primary bony sarcomas, and less than 5% of those with soft-tissue sarcomas of the shoulder, require a forequarter amputation.

Today, forequarter amputation generally is performed only for extremely large tumors arising from the proximal humerus or scapula. These lesions are usually associated with fracture, tumor–hemorrhage, fungation, infection, and/or axillary and brachial plexus involvement.

Preoperative evaluation entails examination and imaging of the potential margins of resection, particularly the underlying chest wall, paraspinal muscles, thoracic outlet and the posterior triangle of the neck. Extension into any of these areas may make it impossible to obtain surgical margins. At surgery the patient is placed in a semilateral position. The utilitarian surgical incision (see Chapter 33) is used. A semi-lateral position is used at surgery. The axillary vessels are exposed anteriorly and ligated, and the posterior structures are then released from the large, posterior, midline-based incision. Rehabilitation is begun prior to discharge from the hospital. Prostheses are available and are generally used only for cosmesis.

INTRODUCTION

Forequarter amputation (interscapulothoracic amputation) entails the surgical removal of the entire upper extremity and shoulder girdle, including the scapula and a portion of the clavicle.^{1,2} Traditionally forequarter amputations were most commonly performed for high-grade bone sarcomas of the proximal humerus and scapula (Figure 17.1). The proximal humerus is the third most common site for osteosarcomas, and these tumors are the most common primary malignancy of the proximal humerus. Chondrosarcomas and Ewing's sarcoma tend to occur in the scapula.

Until the 1970s most of these tumors were treated by forequarter amputation. In addition, some soft-tissue sarcomas of the periscapular and axillary area require forequarter amputation for local control due to neurovascular involvement.

Fortunately, forequarter amputation is rarely performed today. Approximately 90–95% of patients with bony sarcomas of the shoulder girdle can be treated with limb-sparing resection and adjuvant therapy, following the guidelines outlined in this book. Today, the most common indication for amputation of a proximal humeral osteosarcoma is failure to respond to induction chemotherapy and/or tumor progression. Finally, although rare, soft-tissue sarcomas of the supraclavicular or infraclavicular portion of the brachial plexus, and tumors involving the axillary vessels, still are best managed by a forequarter amputation.

UNIQUE ANATOMIC CONSIDERATIONS

The upper extremity and scapula are attached to the upper torso and chest wall by the rhomboid, levator scapulae, trapezius, pectoralis major and minor, latissimus dorsi, teres major, and serratus anterior muscles. During a forequarter amputation these muscles must be transected. The most significant structures that must be evaluated prior to surgery are the axillary and brachial vessels and the adjacent infraclavicular portion of the brachial plexus. These structures pass below the midportion of the clavicle and down the arm adjacent to the inferior border of the coracobrachialis muscle. The coracoid can be easily palpated to identify the brachial plexus and axillary vessels that pass just inferior to it and lie below the deltopectoral fascia. The axillary vessels are routinely evaluated in order to determine the segment that can be safely transected, especially since large tumors may come close to the thoracic outlet.

Other important structures that must be evaluated prior to amputation are the posterior triangle of the neck, the adjacent paraspinal (thoracic) musculature, and the underlying chest wall. Tumors of the

periscapular area may easily extend into these structures. Involvement of these structures makes an amputation inadvisable because negative margins may not be attainable.

STAGING STUDIES

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

These studies accurately evaluate the potential soft-tissue margins; i.e. the neck, paraspinal muscles and chest wall.

Angiography

Angiography is extremely helpful in determining the anatomic position of the axillary and/or brachial vessels, and evaluating whether these structures are involved by tumor. Occasionally, anomalies (e.g. a duplicate axillary artery) are identified. Angiography also makes it possible to accurately determine the level of ligation of the axillary vessels.

Venography

No imaging studies can accurately determine whether the brachial plexus is infiltrated by tumor or whether the vessels and plexus are simply displaced. All of the above imaging studies provide only indirect evidence of tumor extension to the nerves. We have found venography of the axillary veins to be a simple and accurate method of determining brachial plexus involvement. A brachial venogram will show complete obstruction of the main axillary vein when tumor is infiltrating the brachial plexus, whereas a tumor adjacent to, but not infiltrating, the plexus will show venous patency and displacement.

BIOPSY

The biopsy site should follow the incision for a forequarter amputation so that it can be easily removed with the amputation. Care should be taken not to contaminate the large posterior flap, deltopectoral interval, suprascapular area (especially near the neck) and the pectoralis muscle. Large proximal humeral tumors should be biopsied through the anterior deltoid. Scapula tumors should be biopsied along the axillary border, which is in line with the amputation incision.



Figure 17.1 Two different patients requiring a forequarter amputation in lieu of a limb-sparing procedure. (A) A large telangiectatic osteosarcoma of the right proximal humerus that involves the entire shoulder circumferentially. (B) Multiple recurrent tumor nodules following a failed limb-sparing surgical procedure [Tikhoff–Linberg (Type IV) procedure] for a very aggressive multiple recurrent leiomyosarcoma. There are multiple tumor nodules along the entire previous suture line. This patient received radiation therapy prior to amputation.

INDICATIONS AND CONTRAINDICATIONS

The major indications for forequarter amputation are as follows:

1. Unresectable high-grade osteosarcoma (or any other high-grade tumor) of the proximal humerus or the scapula (most commonly, chondrosarcoma).
2. Axillary soft-tissue sarcomas involving the brachial plexus.
3. Recurrent bone or soft-tissue sarcomas following a failed limb-sparing procedure.
4. Some radiation-induced sarcomas of the shoulder girdle.
5. Palliative amputation (primarily due to tumor fungation, infection, or bleeding).
6. Recurrent breast carcinoma involving the brachial plexus.
7. Pathological fracture through a high-grade sarcoma, especially if there is a poor response to induction chemotherapy (Figure 17.2).

Forequarter amputation is contraindicated when tumor extends to the chest wall. It is likewise contraindicated when tumor extends to the paraspinal and posterior triangle of the neck structures, because in this situation negative margins may not be obtained.

SURGICAL GUIDELINES

Several surgical techniques have been described for performing a forequarter amputation. We recommend a semilateral approach. The patient is placed in a lateral position and the majority of the surgery is performed anteriorly. The axillary vessels and brachial plexus are

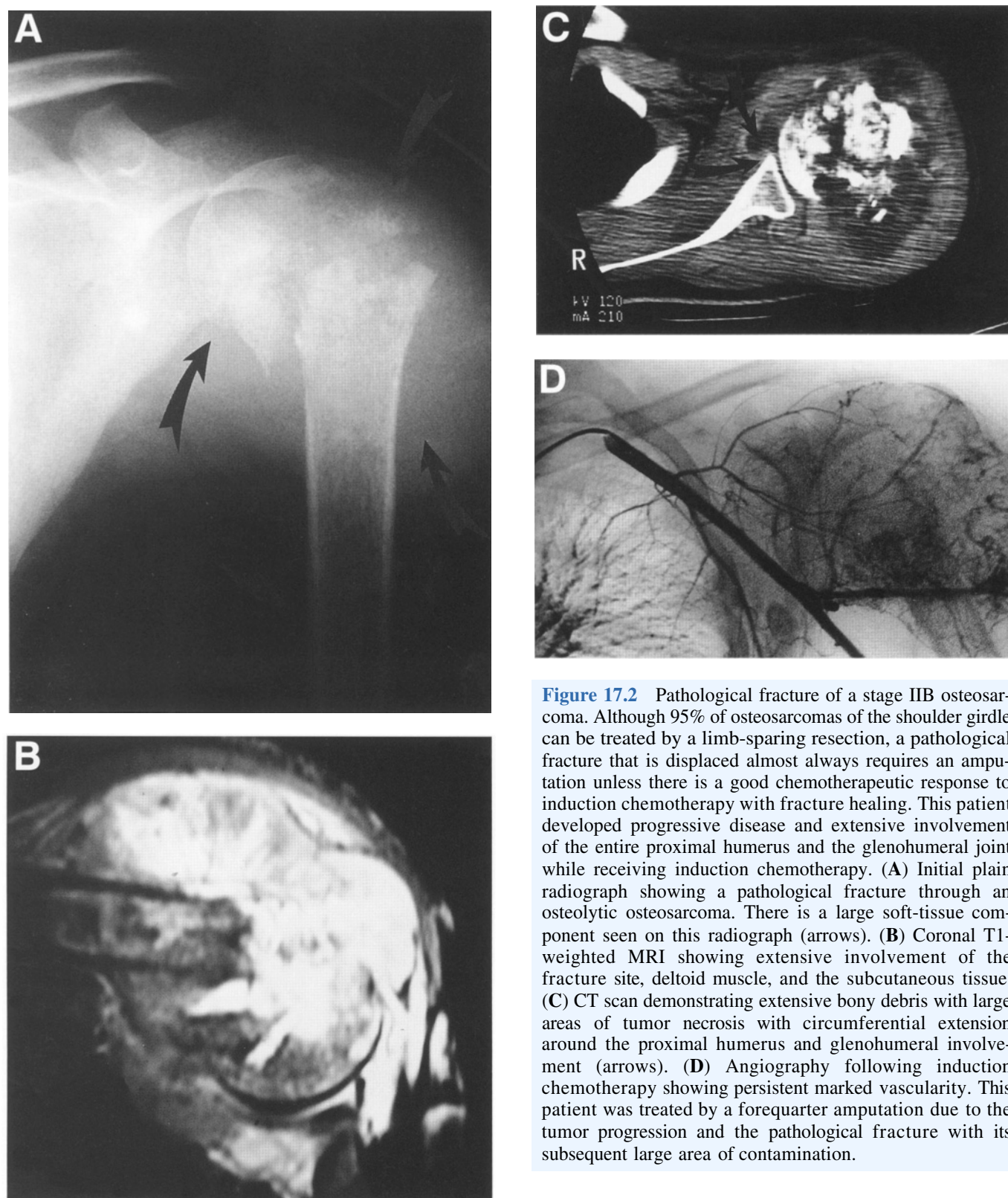


Figure 17.2 Pathological fracture of a stage IIB osteosarcoma. Although 95% of osteosarcomas of the shoulder girdle can be treated by a limb-sparing resection, a pathological fracture that is displaced almost always requires an amputation unless there is a good chemotherapeutic response to induction chemotherapy with fracture healing. This patient developed progressive disease and extensive involvement of the entire proximal humerus and the glenohumeral joint while receiving induction chemotherapy. (A) Initial plain radiograph showing a pathological fracture through an osteolytic osteosarcoma. There is a large soft-tissue component seen on this radiograph (arrows). (B) Coronal T1-weighted MRI showing extensive involvement of the fracture site, deltoid muscle, and the subcutaneous tissue. (C) CT scan demonstrating extensive bony debris with large areas of tumor necrosis with circumferential extension around the proximal humerus and glenohumeral involvement (arrows). (D) Angiography following induction chemotherapy showing persistent marked vascularity. This patient was treated by a forequarter amputation due to the tumor progression and the pathological fracture with its subsequent large area of contamination.

exposed anteriorly and not posteriorly. The posterior approach alone has been found to be unreliable and dangerous for most large tumors of the scapula and suprascapula area. Anterior exposure is especially important when a large tumor has displaced the axillary and subclavian vessels. It would be extremely difficult to identify and avoid harming these structures from a strictly posterior approach.

- We recommend that the anterior limb of the utilitarian incision be utilized to perform an anterior exploration and to mobilize the brachial plexus and axillary nerves.
- Anterior vascular exploration is performed by detaching the pectoralis major muscle from the clavicle. A clavicular osteotomy is performed at the proximal one-third junction. Once these nerves are identified, a Statinski clamp can be placed high along the vessels that lie beneath the clavicle. Surgery can then proceed in an orderly manner.
- The posterior approach is utilized to detach the scapula from the rhomboids, trapezius, and the

levator scapulae and latissimus dorsi muscles. The scapula is lifted from the chest wall by detaching the latissimus dorsi at its lowest points. This exposes the posterior chest wall and makes it possible to perform a manual examination.

- The surgeon can place his or her hand into the axillary space to determine whether there is chest wall or intercostal muscle involvement. If not, the planned amputation can proceed. If there is chest wall involvement, a combined chest wall/forequarter amputation can be performed.
- Axillary incision is made to connect the anterior and posterior incisions.
- The entire forequarter is removed after ligation and transection of the brachial plexus and subclavian vessels.
- The large posterior flap is easily closed over the remaining chest wall defect.
- A marcaine catheter is placed into the remaining brachial plexus for postoperative pain relief. A 28-gauge chest tube is used for drainage for 48–72 h.

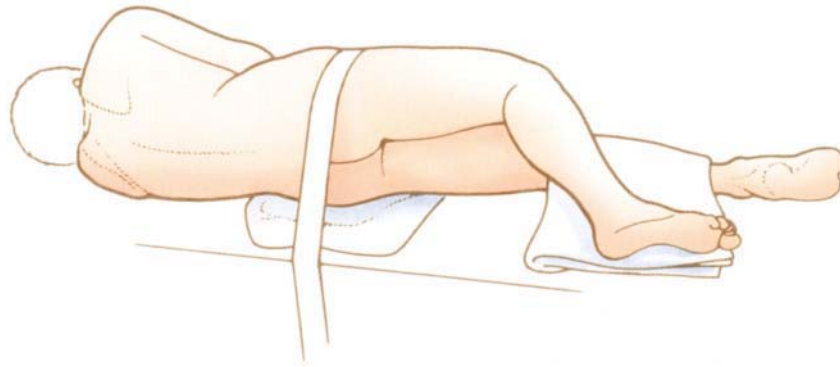


Figure 17.3 Position. Intravenous lines are secured, and a Foley catheter is placed in the bladder. The patient is placed in a full lateral position and secured at the hips with tape. Alternatively, a VAC pack can be used to secure the torso. An axillary roll is placed under the axilla to allow full excursion of the chest, and a sponge-rubber pad is placed under the hip to prevent ischemic damage to the skin in this area. The skin is prepared, and the tumor-bearing extremity is draped free.

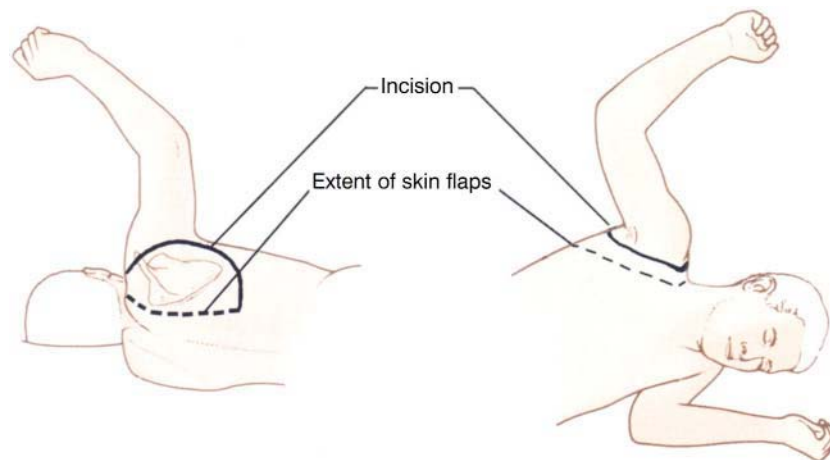


Figure 17.4 Incision and skin flaps. The incision starts over the clavicle about 1 inch lateral to the sternoclavicular joint. The medial line of incision is in or near the deltopectoral groove; the lateral line crosses the tip of the acromion. These lines meet below the axilla; the surgeon must be sure to excise all of the skin bearing axillary hair. The position of the lines of excision will vary with tumors in different positions. In the patient shown (in [Figure 17.1A](#)), a hematoma over the deltoid muscle anteriorly required that the anterior skin flap be moved further forward than usual. Because of the excellent blood supply to the skin in this region, long anterior or posterior flaps uniformly survive even though closed under considerable tension. If a tumor mass has extensive skin involvement, the flaps that remain should be secured to the chest wall with absorbable suture material, and the remaining defect covered with split-thickness skin graft.

The surgeon stands posterior to the patient. The posterior skin flap is usually constructed first. The flaps are constructed as thick as possible so that dissection is usually on the muscle fascia. It is usually possible to widely sacrifice skin around a tumor mass or a previous biopsy site so that thin skin flaps are usually unnecessary. Hematoma that results from the biopsy should always be included within the operative specimen. The posterior skin flap is elevated back to the medial border of the scapula. If a long posterior skin flap is required, this dissection may go back to the vertebral spines. The anterior skin flap is elevated back to the anterior axillary line. If a long anterior flap is required, the flap can extend back to the mid-sternum.

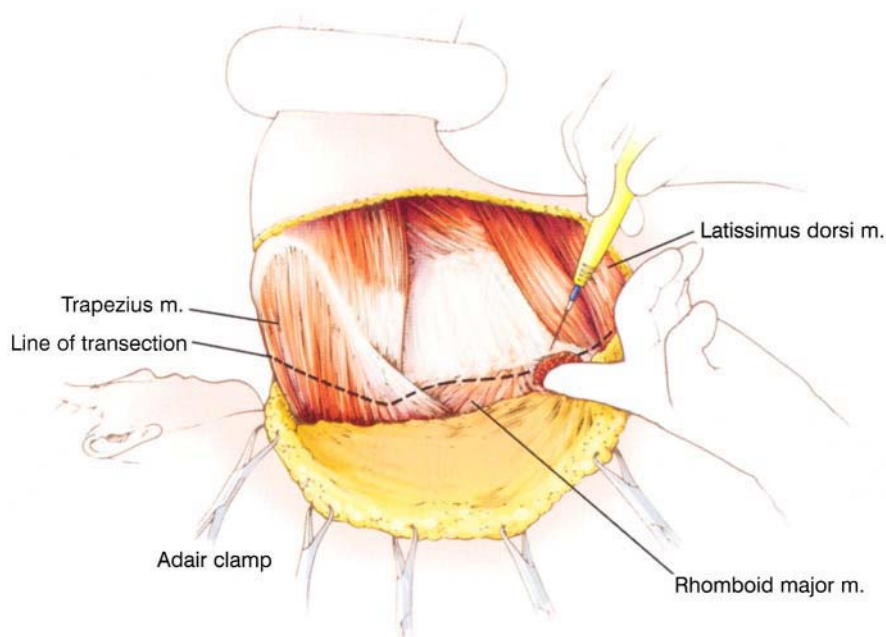


Figure 17.5 Transection of posterior muscular attachments of the scapula. An incision in the deep fascia at the mid-portion of the posterior border of the scapula allows the surgeon to pass a finger beneath the scapula. Electrocautery is then used to divide the rhomboid muscles (major and minor), trapezius muscle, and levator scapulae muscles as they insert onto the scapula. Moving caudally, the surgeon transects the latissimus dorsi.

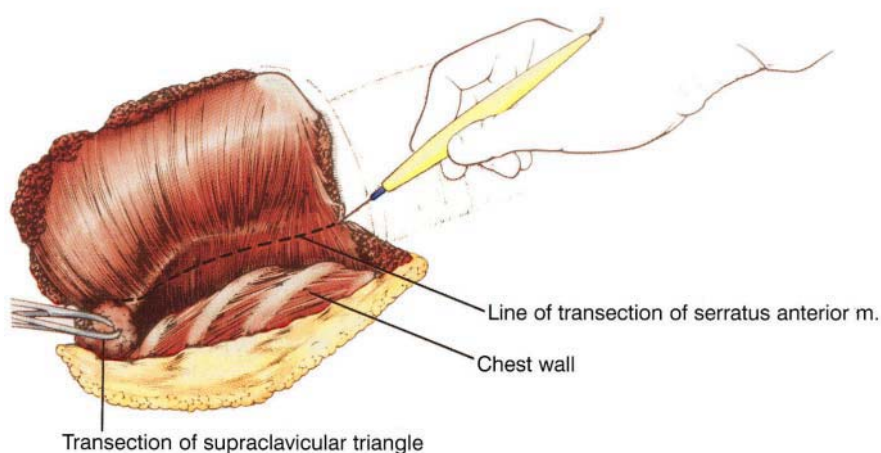


Figure 17.6 Division of contents of the supraclavicular triangle and serratus anterior muscle. Elevation of the scapula allows the structures of the supraclavicular triangle to be divided between hemostats. This includes the transverse cervical and transverse scapular arteries, many lymphatic channels, and the omohyoid muscle. Care is taken to sweep the contents of the axilla into the surgical specimen. The serratus anterior muscle is divided at its origin on the chest wall. This clearly exposes the neurovascular bundle.

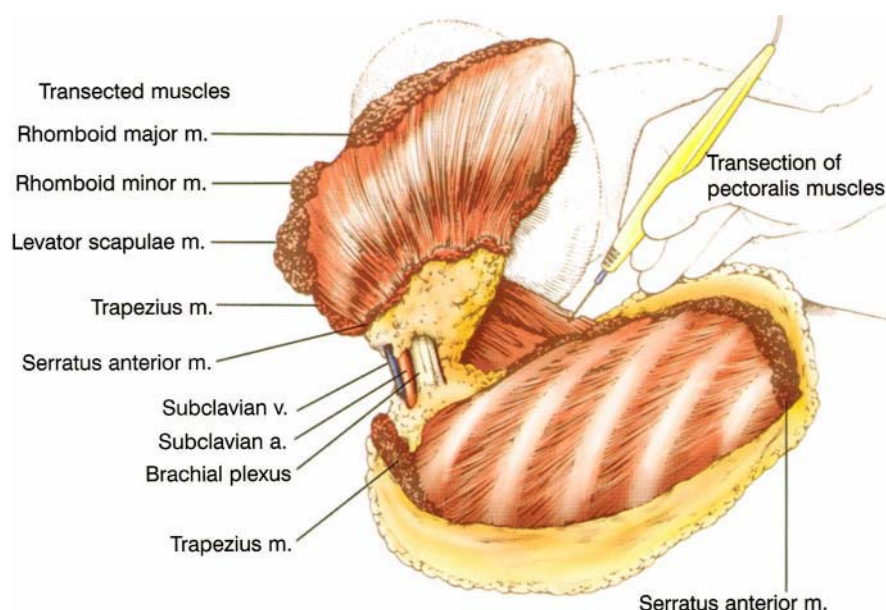


Figure 17.7 Transection of the pectoralis muscles, clavicle, and neurovascular bundle. Anteriorly, the pectoralis major and pectoralis minor muscles are divided. Elevation of the inferior angle of the scapula allows these muscles to be divided under tension by using electrocautery with minimal blood loss. The clavicular head of the sternocleidomastoid muscle is severed from this bone. The clavicle is disarticulated from its sternoclavicular joint. Subclavian vein and artery are ligated, divided, and then suture-ligated. The three large nerve bundles are ligated and then transected.

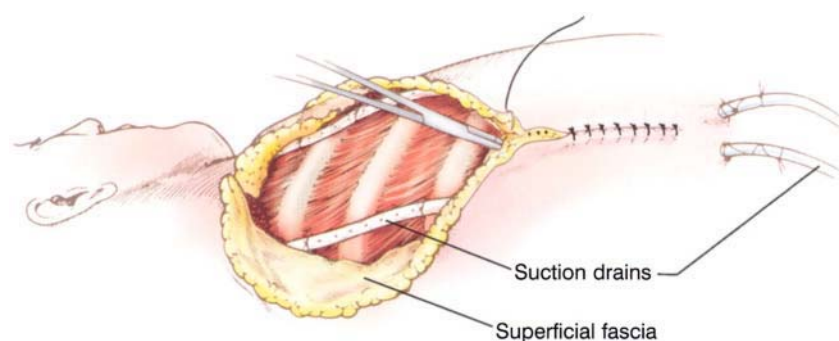


Figure 17.8 Closure. The area is copiously irrigated. Generous suction drainage under the anterior and posterior skin flaps is secured. A marked inequality of the anterior and posterior skin flaps exists. Marked redundancy of the skin may present an unacceptable cosmetic appearance unless the skin flaps are carefully approximated. The mid-portion of the long posterior skin flap is closed to the mid-portion of the anterior flap. Having the closure in this way pleats the longer posterior skin flap and prevents unsightly folds of skin. A two-layered closure of superficial fascia and then skin is used. Suction drains are removed when serous drainage is minimal.

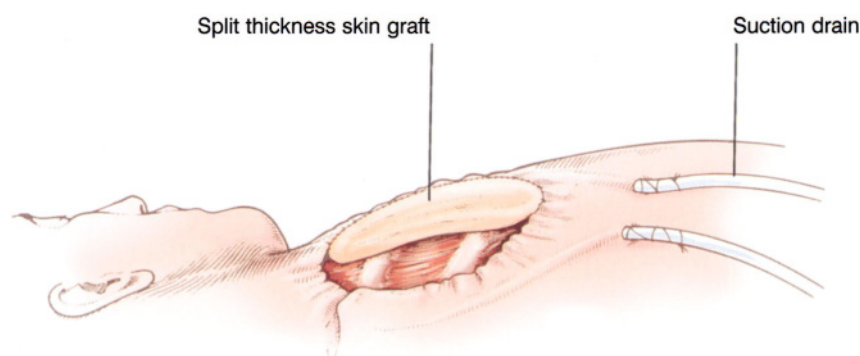


Figure 17.9 Split-thickness graft used to cover the chest wall in tumors with skin infiltration over a wide area.

DISCUSSION

Forequarter amputation is the removal of the entire upper extremity as well as the scapula and a portion of the clavicle. Traditionally, this procedure was the recommended method of treatment of shoulder-girdle sarcomas, both bone and soft-tissue. Today, most osteosarcomas of the proximal humerus are treated with a limb-sparing resection. It is rare for a soft-tissue sarcoma to be unresectable. Amputation is usually required for recurrent soft-tissue sarcomas or those bony lesions that fail induction chemotherapy.

The most common indications for forequarter amputation today are unresectable bone and soft-tissue sarcomas, axillary sarcomas that involve the brachial plexus and axillary artery, recurrent sarcomas following radiation therapy or those bony tumors that progress on induction chemotherapy. Tumor recurrence around the shoulder girdle is a major problem when it occurs. If multiple local resections and radiation therapy fail, the only alternative often is a forequarter amputation. More recently, patients with locally recurrent breast carcinoma (without metastatic disease) that extensively involve the shoulder, the pectoralis muscle, and/or the brachial plexus may require a palliative forequarter amputation.

Before a forequarter amputation is performed, it is important to ascertain that all surgical margins will be free of tumor. Thus, it is important to evaluate the following close anatomic structures that are not removed: the chest wall, posterior triangle of the neck, and the thoracic paraspinal muscles. If these planes are clear, an amputation can proceed.

No imaging studies can adequately determine brachial plexus involvement. Brachial venography can be extremely valuable in determining whether the brachial plexus is involved by tumor or simply displaced. When tumor is infiltrating the brachial plexus, a brachial venogram will show complete obstruction of the main brachial veins and axillary vein. Simple displacement would not occlude the venous structures.

Brachial venography, in conjunction with a careful physical examination, is the key to determining brachial plexus involvement. Patient complaints of nerve pain or weakness, combined with a positive brachial venogram, generally indicates tumor invasion of the brachial plexus, not simple displacement. Nerve pain or actual sensory motor loss, combined with brachial and axillary venography showing an obstruction, is pathognomonic of brachial plexus invasion by tumor. This is a clear indication of the need for forequarter

amputation. The final decision, however, is made intraoperatively after exploring the tumor and the brachial plexus.

Palliative forequarter amputation remains an important procedure in the treatment of large, bulky sarcomas of the shoulder girdle as well as breast carcinomas that recur following multiple procedures and radiation therapy. Unfortunately, a significant number of women develop locally recurrent disease in the axilla, pectoralis major muscle, or of the adjacent clavicle or shoulder girdle. This, combined with previous radiation and the resultant lymphedema, as well as a brachial plexus neuropathy, may often leave the patient with a useless extremity. This combination of recurrent tumor, brachial plexus neuropathy, shoulder-girdle involvement, unresolvable pain, and inevitable tumor fungation, bleeding, and infection requires that a palliative forequarter amputation be performed with individualized types of flaps or skin grafts. This often is required, even in the face of metastatic disease. It is even more appropriate when there is no evidence of metastatic disease; in this case the procedure may be considered curative.

The surgical procedure utilized for palliative forequarter amputation differs from the standard amputation presented in this chapter in that it entails the development of a large posterior fasciocutaneous flap that includes the arm skin, extending from the shoulder to the elbow from the middle to lateral aspects posteriorly. This large flap is extremely vascular and can be rotated to close the chest wall defect. This technique has been utilized in cases of major crush injuries to the upper extremity and shoulder girdle, as well as following massive gunshot wounds. It has found a place in the treatment of the oncological patient when there has been previous radiation therapy to the skin flaps combined with massive recurrent tumor, with or without infection. The outcome of this operative procedure can be satisfactory. The patient is almost immediately relieved of infection and pain and can proceed with the remainder of his/her life on a very functional basis.

Phantom pain (causalgia) is a major problem following high-level amputations. We use an epineural catheter placed into the axillary sheath at the time of surgery and infuse 0.25% marcaine for 3–5 days postoperatively. This decreases postoperative pain and may decrease late causalgia syndromes. Although forequarter amputation is rarely performed today, it can be a life-saving procedure as well as providing a long-term palliative benefit.

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Above-elbow and Below-elbow Amputations

Paul Sugarbaker, Jacob Bickels and Martin Malawer

OVERVIEW

Above-elbow amputations are indicated for advanced soft-tissue and bone sarcomas of the forearm; below-elbow amputations are performed for such tumors of the forearm and the hand. The location of the tumor mass on the medial aspect of the distal arm and elbow joint, in close proximity to the main neurovascular bundle, may in large part determine feasibility of a limb-sparing procedure. Above- and below-elbow amputations are performed to achieve wide surgical margins while preserving as much length as possible of the extremity. The level of amputation will vary with the location of the tumor in the forearm, at the elbow joint, and even at the lower portion of the arm.

During the procedure, muscle flaps are tapered and closed tautly in two layers over the cut ends of the bones in order to facilitate mobility. A rigid dressing is applied immediately postoperatively to decrease pain and edema and facilitate maturation of the stump.

INTRODUCTION

Above- and below-elbow amputations are rare procedures because: (1) the distal arm, forearm, and arm are relatively rare locations for soft-tissue and bone tumors; (2) unlike tumors of the buttocks and lower extremities, because of the fact that these locations are exposed, the tumors are noticed in relatively early stages and in most cases are resectable; and (3) administration of preoperative chemotherapy, and especially via the intra-arterial route or using isolated limb perfusion, significantly decreases tumor size and facilitates a limb-sparing procedure. The feasibility of limb-sparing was further augmented by the development of endoprosthetic devices that allow replacement of the distal humerus, proximal ulna, proximal radius, and even the distal radius, and which offer satisfactory function.

Nonetheless, above- and below-elbow amputations retain a definitive role in the management of soft-tissue and bone tumors of the upper extremity. These are required for tumors that cannot be removed with a wide margin. However, rarely should a grade I soft-tissue sarcoma that is not expected to metastasize be initially treated by amputation. In this case, because of the efficacy of adjuvant radiation therapy, even a marginal margin is acceptable. Indications for above- and below-elbow amputations include:

1. *Local recurrence* was once considered a primary indication for amputation. The mere presence of a recurrent sarcoma is no longer an immediate indication for an amputation. The capability to resect the recurrent tumor without compromising the function of the extremity is the determining factor on which the decision to amputate is based.
2. *Major vascular involvement.* The neurovascular bundle within the arm is tightly integrated in a closed anatomic space. The cephalic vein usually provides sufficient collateral flow if the brachial or the axillary vein has to be sacrificed. However, although occasionally the tumor mass can be delicately dissected off the brachial artery, in most cases of vascular involvement the brachial artery is extensively encased and amputation is inevitable.
The compact nature of the vascular supply to the wrist makes involvement of the radial and ulnar arteries likely when a large tumor invades the volar aspect of the distal forearm. In this instance the incidence of morbidity and failure associated with resection and reconstruction using a vascular graft of one of these vessels is prohibitively high.
3. *Major nerve involvement.* In general, one nerve around the arm can be sacrificed and a two-nerve deficit is tolerated. Sacrifice of the three major nerves leaves

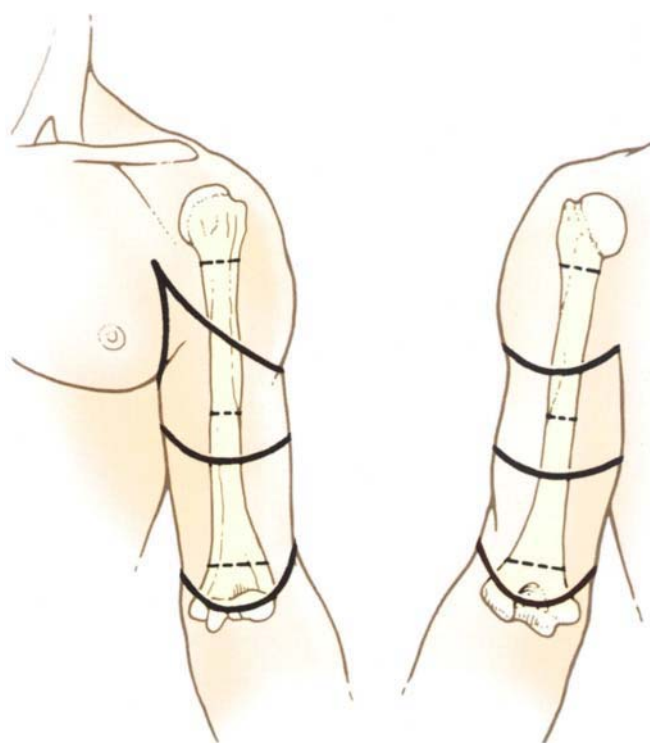


Figure 18.1 Above-elbow amputations are indicated for advanced soft-tissue and bone sarcomas of the forearm. Skin incisions and osteotomy sites for metaphyseal (high), diaphyseal, and supracondylar above-elbow amputations.

the patient with a functionless extremity that is better off amputated. Nerve grafting for replacement of a section of the median, radial, or ulnar nerves is still not associated with satisfactory function.

4. *Extensive soft-tissue contamination* as a result of a pathologic fracture, or an inappropriate biopsy or resection attempt. This is a frequent indication for below-elbow amputation; the anatomy of the hand and lack of true biologic compartments allow both lateral and longitudinal extension of the tumor.
5. *Infection* around the tumor or along the biopsy tract may negate a resection attempt, prohibit the use of a prosthetic device, and delay the administration of adjuvant chemotherapy. Limb-sparing surgery is feasible only if the infection is completely controlled prior to surgery, or if the infected tissues can be completely removed at surgery.

Cancer patients who are candidates for an amputation face a unique psychological problem because not only do they face a threat to their lives, but they will also lose their upper extremity. Besides an obvious aesthetic deficit, loss of the upper extremity, and especially the dominant one, has a profound functional impact. Therefore, the rehabilitation of these patients begins at the time of staging studies. The entire health-care team must develop a trusting and honest relationship with the patient and include him or her at the early stages of all decision making. Building upon this interaction, the patient will be better able to accept the amputation and set realistic goals for return to a productive life. The patient's family, significant peers, and each member of the care team are crucial to this adjustment.

All patients undergoing an amputation may experience phantom limb pain. This is not nearly so severe with distal amputations as it is with proximal amputations. Nonetheless, it should be discussed with the patient prior to surgery. The patient should understand that it is normal and that, if uncomfortable, can be effectively treated (see Chapter 24).

CLINICAL CONSIDERATIONS

Patients requiring above- or below-elbow amputations for a soft-tissue or primary bone sarcoma must undergo complete staging in order to allow the surgeon to determine the level of amputation and extent of soft-tissue resection. Complete staging allows determination of full tumor extent and as a result the site for skin incision, shape of the flaps, and site of osteotomy. The combined use of plain radiography, computed tomography (CT), and magnetic resonance imaging (MRI) is necessary to determine the proximal extent of the intraosseous and soft-tissue components of the tumor. In general, the more proximal of the two levels of involvement (i.e. bone or soft tissue) determines the level of amputation.

Above-elbow amputations can be metaphyseal (high), diaphyseal, or supracondylar (Figure 18.1). High above-elbow amputations are those proximal to the deltoid tuberosity. Patients who undergo amputation proximal to the insertions of the deltoid and pectoralis major muscles have far greater difficulties adjusting to their prosthesis than do those who have undergone a more distal amputation. Below-elbow amputations should preserve the maximal length of both radius and ulna. While tumors of the hand are treated by a standard below-elbow amputation, performed through the distal third of the forearm, tumors of the distal forearm require a higher amputation and warrant special consideration (Figure 18.2). A minimum of 2.5–3 cm of bony stump, measured from the radial tuberosity, is required to



Figure 18.2 Below-elbow amputations are indicated for advanced soft-tissue and bone tumors of the forearm and hand. Skin incision and osteotomy site for below-elbow amputation.

preserve function. Additional length in a very short stump can be obtained by releasing the biceps tendon; adequate flexion of the stump will be provided by the brachialis muscle.

SURGICAL TECHNIQUE

The patient is supine with the ipsilateral shoulder slightly elevated. Standard anterior/posterior "fish-mouth" flaps are used. Occasionally, medial-lateral flaps are needed. Because of the excellent blood supply to the upper extremity, wound healing is rarely a problem.

The skin and superficial fascia are divided perpendicular to the skin surface (Figure 18.3). Large blood vessels are ligated in continuity and then suture-ligated. The nerves are handled delicately. They are pulled approximately 2 cm from their muscular bed, doubly ligated with nonabsorbable monofilament suture, and cut with a knife. Muscles are transected



Figure 18.3 The skin and superficial fascia are divided perpendicular to the skin surface.

according to the flap design and the humerus or the radius and ulna are cut at the appropriate location, as determined by the preoperative imaging studies (Figure 18.4). The radius and ulna are transected at equal lengths.

For optimal function of the stump, it is important that muscle groups will be positioned tightly and securely over the transected bone ends (Figure 18.5). Myodesis is reinforced by Dacron tapes, passed through drill-holes made in the cut end of the bone. Superficial fascia and skin are closed over closed-suction drains (Figures 18.6 and 18.7).

A rigid dressing is used to decrease postoperative pain and edema (Figure 18.8). Care must be taken to adequately protect the skin that directly overlies the bone. Stump edema is rarely a significant problem in the upper extremity and prosthesis training should begin as soon as possible after surgery.

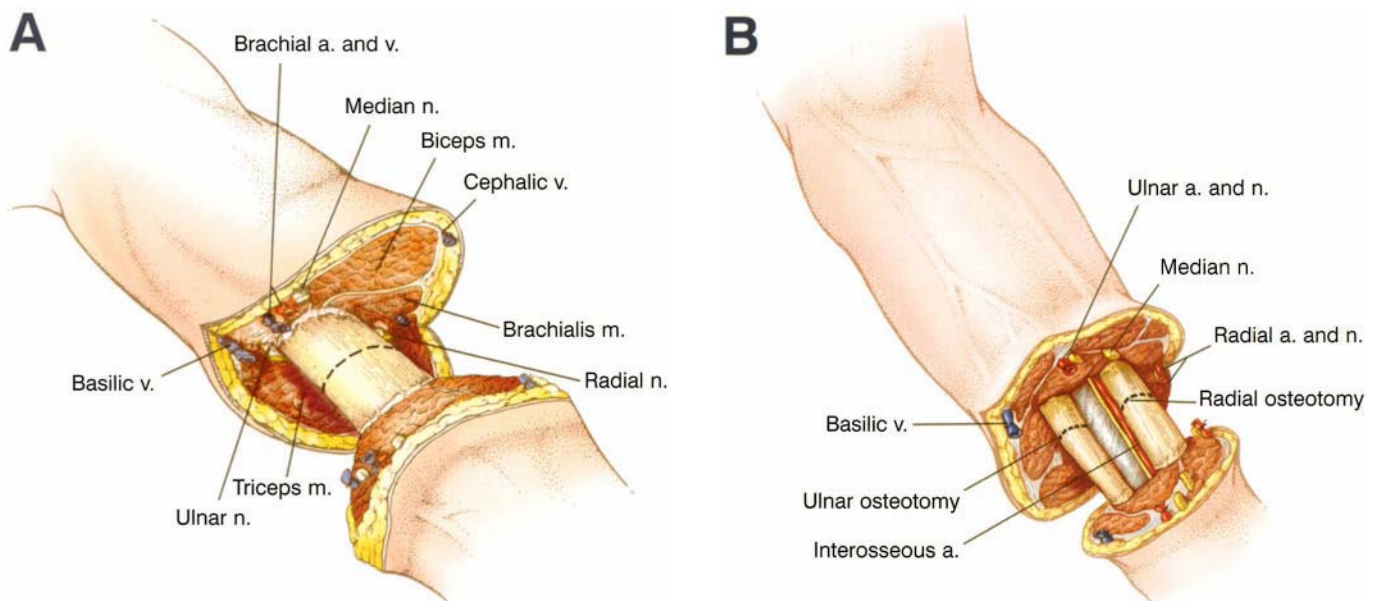


Figure 18.4 Osteotomies are performed at the appropriate location, as determined by the preoperative imaging studies: (A) above-elbow amputation, (B) below-elbow amputation. The radius and ulna are transected at equal lengths.

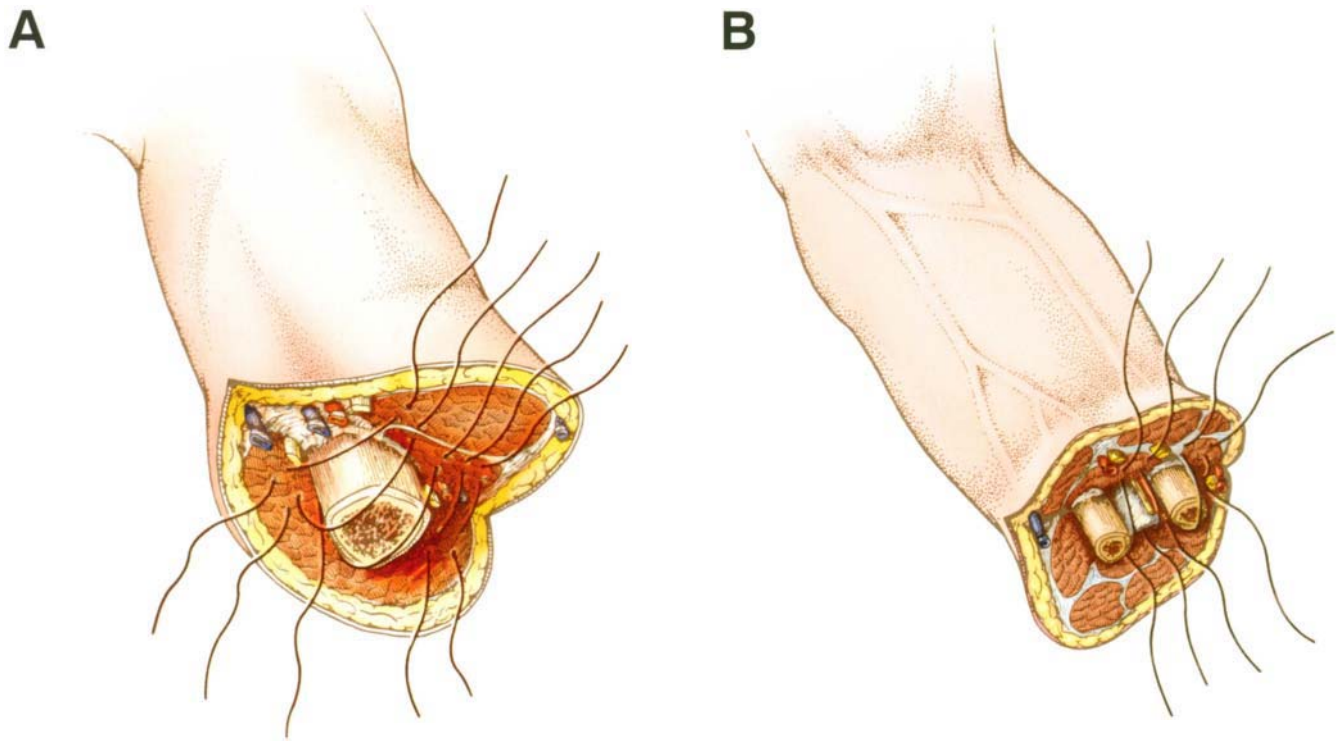


Figure 18.5 Muscle groups are positioned tightly and securely over the transected bone ends: (A) above-elbow amputation, (B) below-elbow amputation.

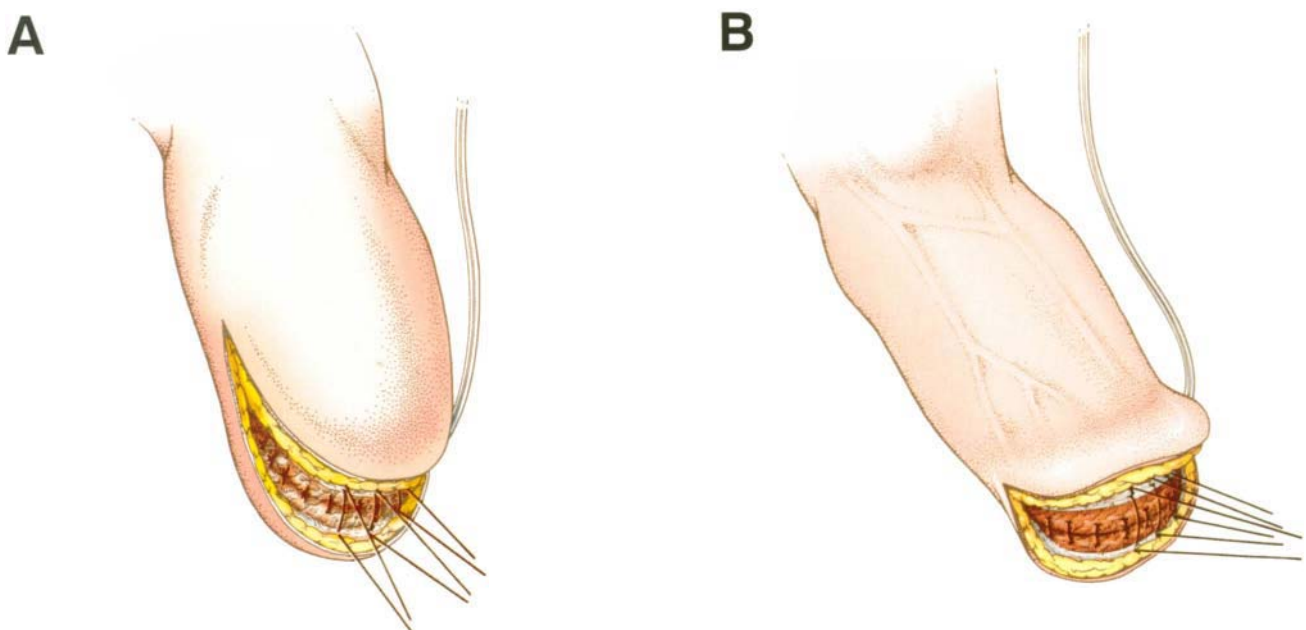


Figure 18.6 Superficial fascia and skin are closed over closed-suction drains: (A) above-elbow amputation, (B) below-elbow amputation.

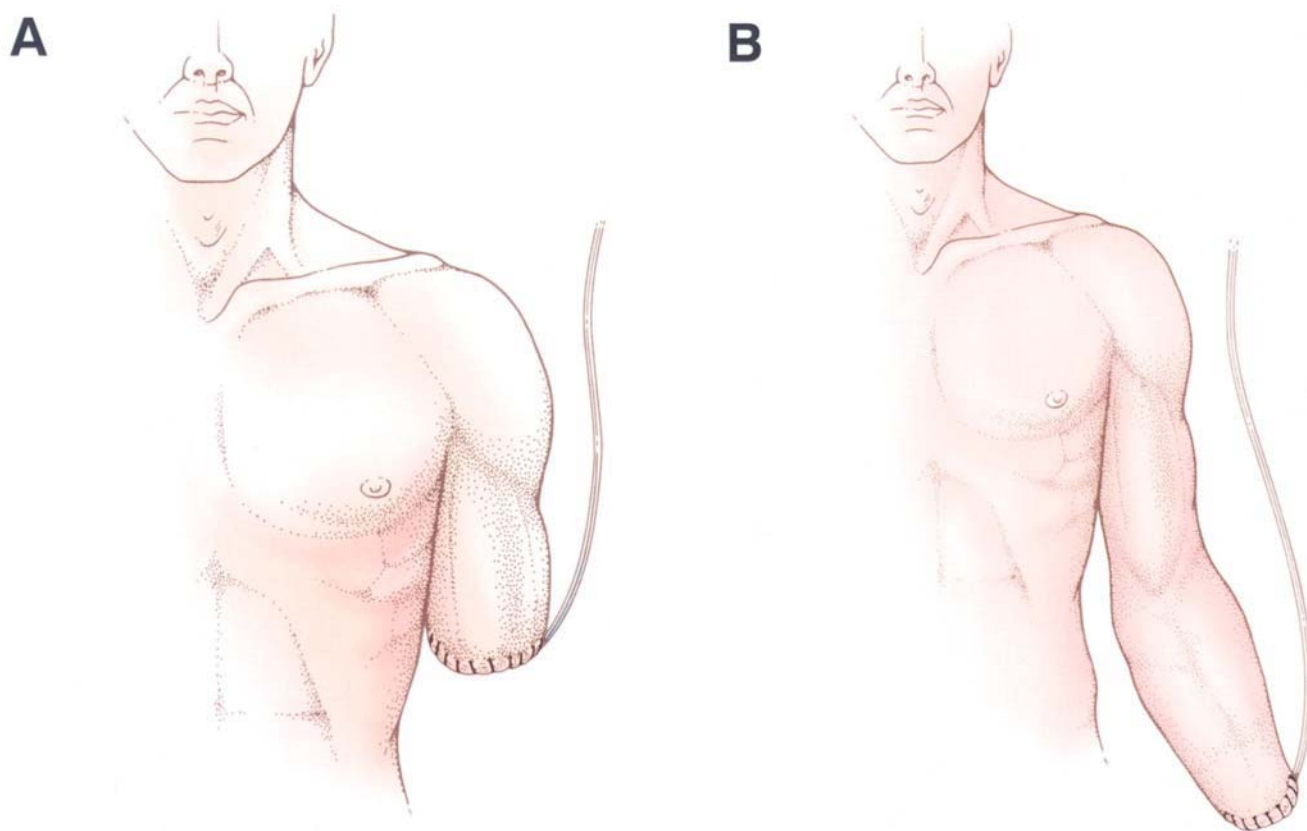


Figure 18.7 Final closure for (A) above-elbow amputation, (B) below-elbow amputation with closed-suction drains.

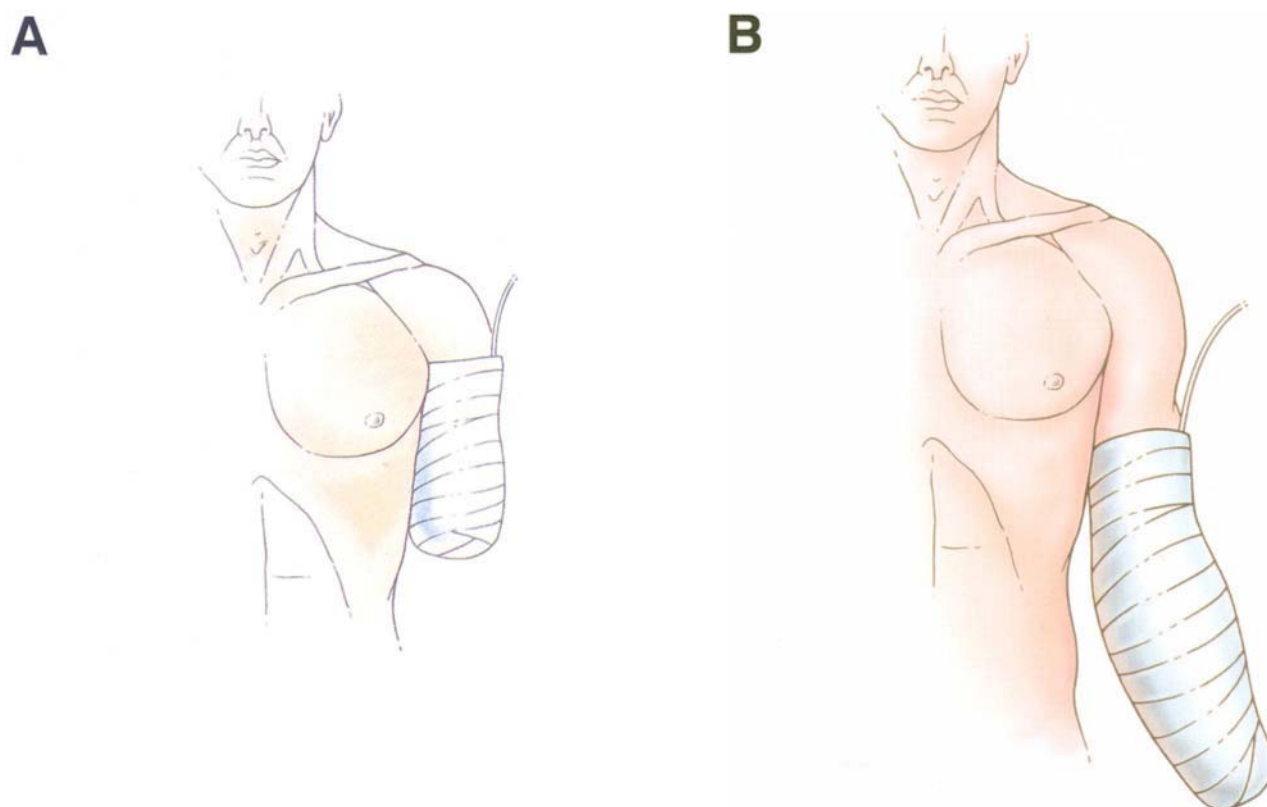


Figure 18.8 A rigid dressing is used to decrease postoperative pain and edema: (A) above-elbow amputation, (B) below-elbow amputation.

Anterior Flap Hemipelvectomy

Martin Malawer, Paul Sugarbaker and Robert Henshaw

OVERVIEW

The anterior flap hemipelvectomy is a modified version of the classical posterior flap hemipelvectomy. Instead of utilizing the traditional posterior skin flap of the gluteal region, a myocutaneous flap from the anterior thigh is used to close the peritoneum following amputation through the sacroiliac joint and the pubic symphysis. This modification has permitted the treatment of difficult buttock and pelvic tumors where the posterior flap was involved and/or contaminated by tumor. This technique offers patients, initially thought to be incurable by standard technique, a good oncological procedure. The anterior myocutaneous flap consists of a portion or the entire quadriceps muscle group on its vascular pedicle, the superficial femoral artery. This flap covers the entire peritoneal surface and generally heals with minimal problems.

INTRODUCTION

Patients with extensive soft-tissue sarcomas of the buttock or bone sarcomas of the pelvis that extend posteriorly, once thought to be incurable by standard posterior flap hemipelvectomy, can often be treated with an anterior flap hemipelvectomy (Figure 19.1). The procedure, which originally entailed use of an anterior skin flap raised off of a portion of the superficial femoral vessels,¹ was later modified to include a full-thickness myocutaneous flap raised from the anterior thigh.^{2,3} This procedure may also be indicated following failed attempts at limb-sparing surgery,⁴ as well as for patients with nononcologic indications for amputation (e.g. uncontrollable sepsis from sacral or trochanteric osteomyelitis). The major advantage of anterior flap hemipelvectomy is the creation of a large vascularized myocutaneous flap that is ideal for closure of significant posterior defects. As much of the anterior thigh compartment may be saved as needed, depending on the size of the defect being closed. As always, careful patient selection is critical in ensuring that an acceptable outcome is achieved. For example, elderly patients and diabetics with silent atherosclerotic disease of femoral vessels must be carefully evaluated with preoperative angiography. The suitability of this procedure may also be limited by the anatomic location of the tumor.

CLINICAL CONSIDERATIONS

Sugarbaker^{3,6} and others^{1-5,7-9} have shown the utility of a myocutaneous pedicle flap based upon the femoral vessels and anterior compartment of the thigh for closure of the wound in patients with tumors involving the posterior buttock structures (Figure 19.2). This procedure has been termed an "anterior flap" hemipelvectomy to distinguish it from the more common "posterior flap" hemipelvectomy. Anterior flap hemipelvectomy is indicated for tumors involving the buttock that cannot be resected with a less radical procedure. Patients who have failed prior attempts at limb-sparing surgery, with or without radiation, or who have tumors that primarily involve the posterior thigh and sciatic nerve, are also candidates for this procedure (Figure 19.3). Nononcologic indications include selected paraplegics with uncontrollable chronic osteomyelitis of the pelvis and/or hip joint. The primary advantage of this procedure in all of the above cases is that the anterior flap raised from the thigh can be used to reconstruct an enormous posterior defect with little risk of flap necrosis. Patients who are expected to require substantial doses of radiation postoperatively should be considered for this procedure whenever possible, since the well-vascularized myocutaneous flap tolerates radiation well.

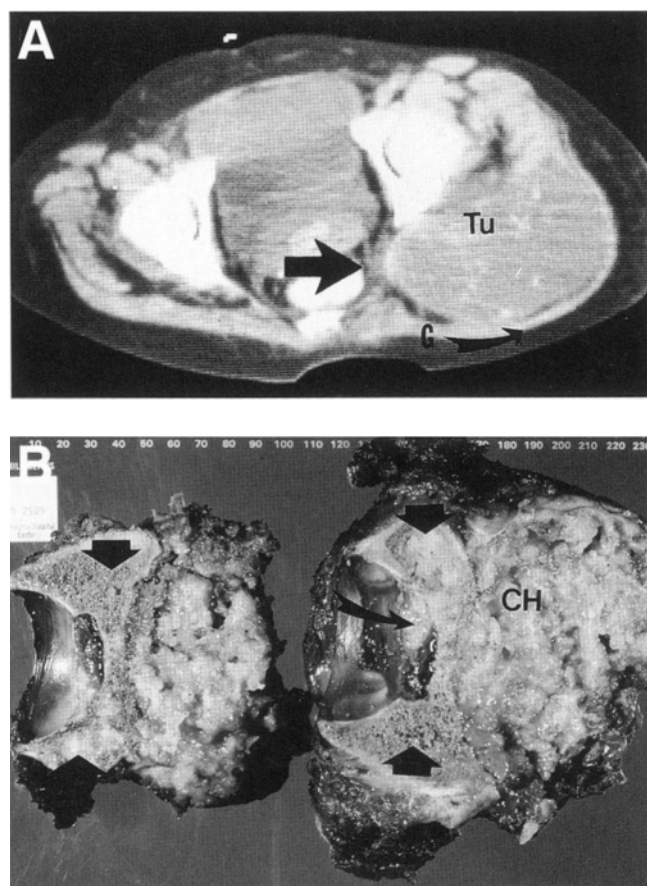
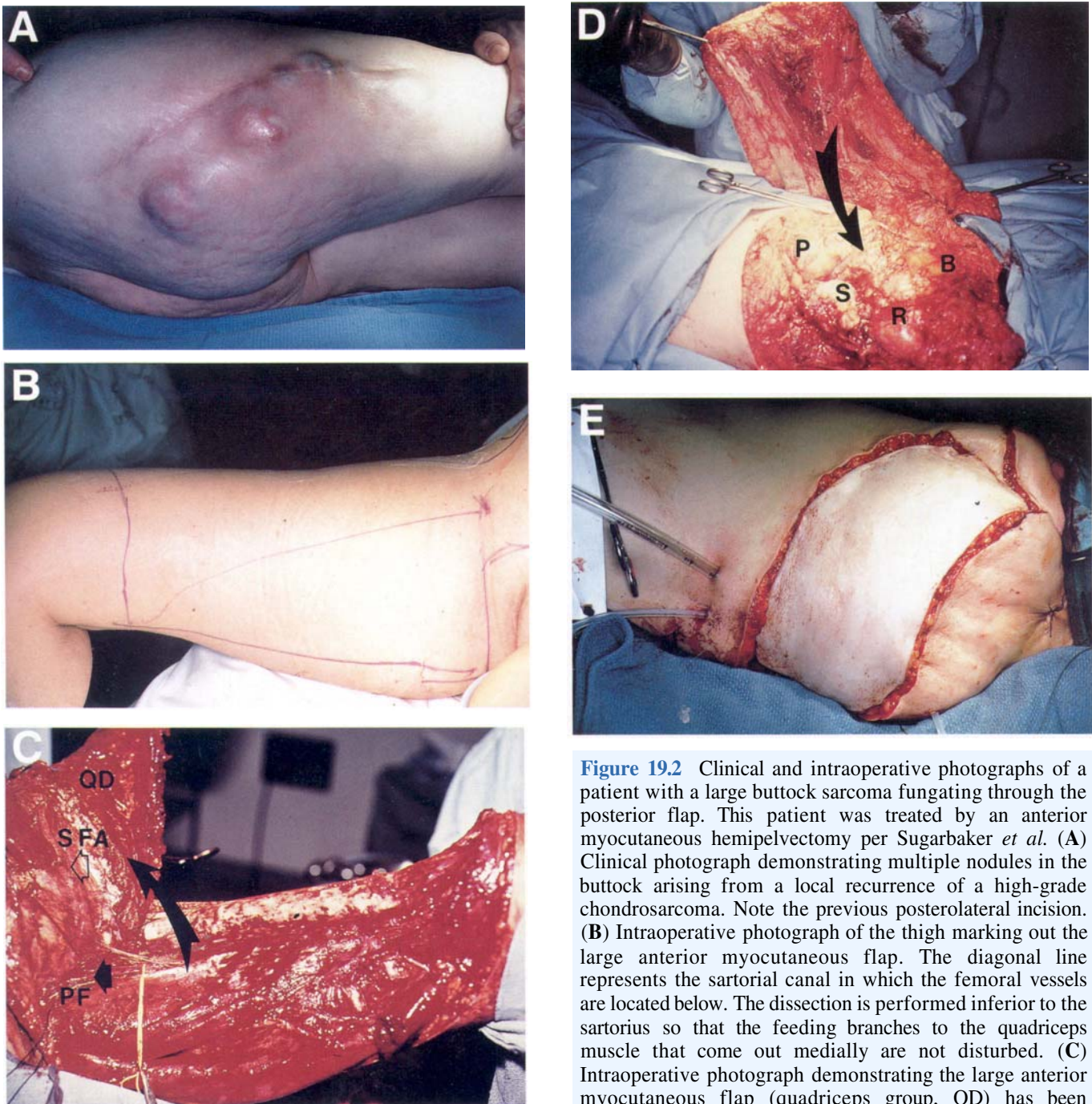


Figure 19.1 (A) Large extraosseous chondrosarcoma of the buttocks (Tu) with a thin rim of gluteus maximus muscle remaining (G) showing early intrapelvic extension through the sciatic notch (large arrow). This is a typical mechanism of tumor extension into the pelvis and usually indicates the need for a hemipelvectomy. (B) Partial sectioning of a gross specimen following a hemipelvectomy. Chondrosarcoma (CH) can be seen (small and curved arrows) extending below the ilium into the sciatic notch and involving the adjacent sciatic nerve. Tumor involvement of the sciatic notch almost invariably involves the gluteal vessels as well as the exiting sciatic nerve. This patient was treated with an anterior flap hemipelvectomy.

Because of the vascular nature of this flap, the surgical wound heals rapidly in the vast majority of patients. Accordingly, the 10–30% risk of ischemic necrosis associated with posterior flap hemipelvectomy is not seen with an anterior flap procedure. Likewise, the risk of subsequent infection in the postoperative period is markedly reduced. Great care must be taken not to dissect or shear the subcutaneous tissue and skin overlying the quadriceps during the creation of the flap, because this will compromise the cutaneous circulation.

Rehabilitative considerations and the risk of phantom pain are similar to those associated with other types



of hemipelvectomies. Because of the rapid healing seen with this type of flap, prosthetic fitting may be performed earlier. The cushioning effect of the quadriceps muscle may significantly reduce tenderness along the cut edge of the sacrum.

UNIQUE ANATOMIC CONSIDERATIONS

The surgeon must be familiar with the pelvic anatomy as well as the thigh musculature and femoral vessels. The anatomic key to this procedure is the major

Figure 19.2 Clinical and intraoperative photographs of a patient with a large buttock sarcoma fungating through the posterior flap. This patient was treated by an anterior myocutaneous hemipelvectomy per Sugarbaker *et al.* (A) Clinical photograph demonstrating multiple nodules in the buttock arising from a local recurrence of a high-grade chondrosarcoma. Note the previous posterolateral incision. (B) Intraoperative photograph of the thigh marking out the large anterior myocutaneous flap. The diagonal line represents the sartorial canal in which the femoral vessels are located below. The dissection is performed inferior to the sartorius so that the feeding branches to the quadriceps muscle that come out medially are not disturbed. (C) Intraoperative photograph demonstrating the large anterior myocutaneous flap (quadriceps group, QD) has been elevated off of the quadriceps muscle. The vessel loop shows the profundus vessel (PF) that is now ready to be ligated to permit the flap to be elevated above the pelvis. The superficial femoral artery (SFA, open arrow) remains on the quadriceps muscle as the major pedicle (large arrow). (D) Intraoperative photograph following amputation and ligation of the profundus vessel and complete elevation of the anterior myocutaneous flap (P, peritoneum; S, sacrum; R, rectum; B, bladder; arrow indicates major pedicle). (E) Intraoperative photographs show the flap has been rotated to close over the large defect. Note the flap can be positioned in many directions. It is important that the underlying iliac and external iliac arteries and veins are not twisted when the flap is set into the defect.



Figure 19.3 Gross specimen following an anterior flap hemipelvectomy. Note there is a large extraosseous tumor mass in the buttock region as well as in the adductor region. This patient had been treated by an IM rod mistakenly for a benign lesion. The rod has been removed and the tumor tract can be seen. In addition there is a pathologic fracture present (Fx). Small arrow shows the intramedullary tract. This is one of the more common indications for anterior flap hemipelvectomies; that is, mistaking posterior IM rodding of primary malignancies.

vascular pedicle of the pelvis and extremity (Figure 19.2C). Oncologic considerations for tumor involvement of the bone or soft tissues in the pelvis are identical to those discussed in the chapter on posterior flap hemipelvectomy.

The external iliac vessels leave the pelvis and cross through the femoral triangle, where they become the common femoral vessels. A single branch supplying the iliac crest may be encountered along the medial aspect of the external iliac vessel just below the inguinal ligament. The superficial femoral vessels travel underneath the sartorius muscle along most of the length of the thigh; they pass through the adductor hiatus and become the popliteal vessels behind the knee. The major branch in the femoral triangle is the profunda femoris, which arises from the posterior aspect of the superficial femoral vessel and passes deep to the posterior surface of the femur. Ligation of the profunda femoris is required to elevate the anterior flap. The common femoral and superficial femoral vessels are preserved.

The (four) quadriceps muscles, the adductor muscles, and the sartorius muscle all have a vascular supply that arises from pedicles off of the superficial femoral artery. Perforating branches from the profundus are present in the vastus lateralis and may be encountered as they pass through the intramuscular septum. The entire anterior and medial compartments can be elevated off of the femur by dividing the quadriceps tendon above the patella and peeling the full-thickness myocutaneous flap off of the anterior femoral periosteum. To prevent hemorrhage, care must be taken to properly ligate all perforating vessels, as well as the superficial femoral vessels, at the level of the adductor hiatus.

Division of the skin at the inguinal canal and skeletonization of the external iliac vessels permit the entire flap to be rotated as necessary to cover the defect created by the amputation. Use of this flap for closure results in improved cosmesis and facilitates fitting of a prosthesis for an improved functional result. In addition, this flap permits radiation therapy to the remaining pelvis without any wound complications. The nature of the flap available for closure permits greater posterior resection than that possible during a traditional posterior flap hemipelvectomy. The entire buttock compartment (i.e. the gluteal muscles, sciatic nerve, sacrospinous ligaments and sacral alar) can be safely removed.

IMAGING/STAGING STUDIES

In addition to the routine radiographic evaluation of the pelvis (x-rays, CT/MRI scans and bone scans) necessary to determine the suitability of a hemipelvectomy, angiography of the femoral vessels should be considered essential for patients undergoing anterior flap hemipelvectomy. The variable nature of the profunda femoris, as well as the frequent presence of silent atherosclerosis of the superficial femoral artery in elderly patients or in patients with a history of smoking, can greatly affect the outcome of this procedure. In addition, visualization of the pelvic vessels can help to ensure that they are not involved with the tumor.

CT and MRI are required to determine if the tumor involves the sacrum or the vertebra. Spinal involvement is a contraindication to this procedure.

SURGICAL GUIDELINES

1. Positioning the patient (lateral).
2. Ilioinguinal dissection and pelvic exploration.
3. Dissection and ligation of the internal (hypogastric) iliac vessels.
4. Elevation of anterior thigh flap with external iliac/superficial femoral artery.

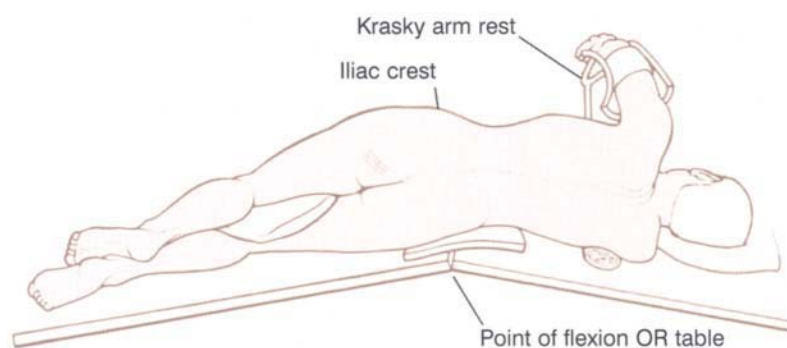


Figure 19.4 Position. Preoperative preparations include correction of blood deficits and a complete bowel preparation. In females the vagina is also prepared. Venous and arterial lines are secured, and a drainage catheter is placed in the bladder. After being placed supine on the operating table, the patient is rolled into the lateral position with the iliac crest at the flexion point of the table. As the patient is positioned, a cushion is placed beneath the right iliac crest and greater trochanter to prevent pressure necrosis of the skin. Padding beneath the right axilla is used to allow full excursion of the chest wall and as prophylaxis against injury to the brachial plexus. The left arm is placed on a Krasky arm rest. An elastic wrapping or a support stocking is used to prevent blood pooling in the right lower extremity. The operating room table is flexed to open the angle between the crest of the ilium and the lumbar vertebra. The anus is sutured shut. The left lower extremity is prepared and draped free with the skin exposed circumferentially from the knee to the iliac crest.

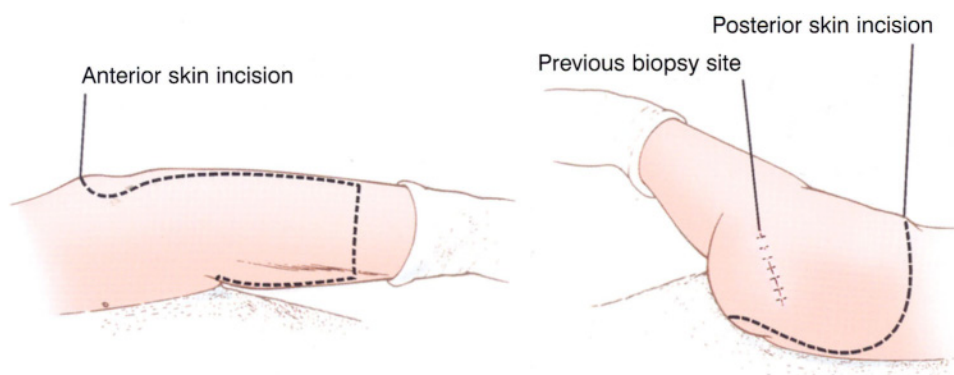


Figure 19.5 Incision. It is critical to determine before the operation that the myocutaneous flap created from the tissue overlying the quadriceps muscle will cover the operative defect created in the buttock. The location of the proposed incision is mapped out with a marking pen and the width and length of the flap compared with the anticipated defect in the buttock. Once it is ascertained that the flap is adequate to cover the defect, the remainder of the incision is determined. First, draw the location of the incision medial to the tumor at or near the midline posteriorly above the anus. Superiorly and laterally the incision should parallel the wing of the ilium to the anterior superior iliac spine. It then continues distally along the midpoint of the lateral aspect of the thigh to the junction of the lower and middle thirds of the thigh.

The medial incision courses 2–3 cm lateral to the anus, then anteriorly in the gluteal crease toward the pubic tubercle. It then continues along the midpoint of the thigh to the junction of the lower and middle thirds of the thigh. The two longitudinal incisions extending along the lateral and medial aspects of the thigh are connected by a transverse incision over the anterior aspect of the thigh. The location of this transverse incision determines the length of the myocutaneous flap. Hence it should be ascertained that the transverse incision is positioned so the tip of the flap will extend to the level of the iliac crest.

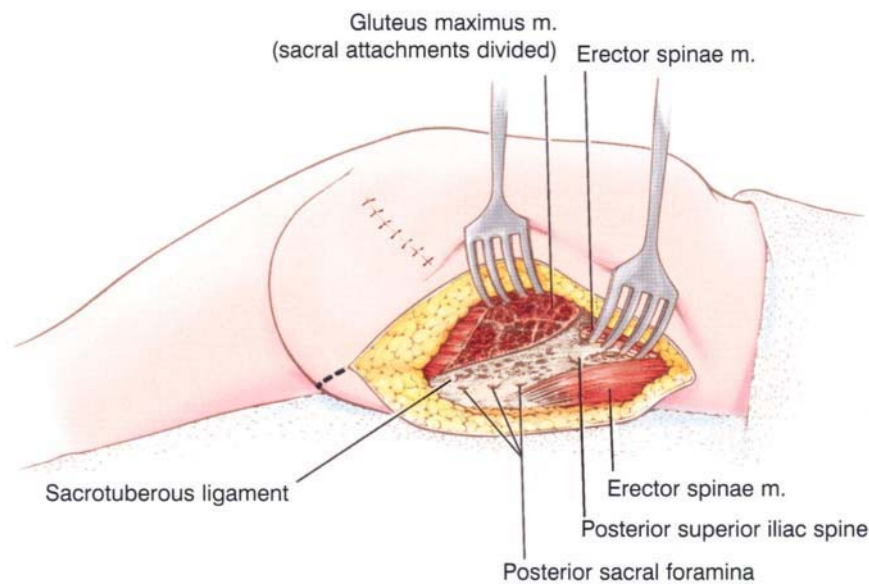


Figure 19.6 Posterior incision to determine operability. In excision of buttock tumors the medial margin of the tumor is usually the closest one to the line of excision. Therefore the dissection should commence medial to the tumor to allow the surgeon to assess operability before completion of the amputation is required. The initial incision is made superficial to the sacrum in the midline, through fascia to the midsacral spines. A cuff of skin 2–3 cm in length should be preserved around the anus. The sacral attachments of the gluteus maximus and erector spinae muscles are divided from their origins between the midsacral spines and the dorsal sacral foramina. Biopsies from the medial margin of resection are secured. By removing the outer table from the sacrum, biopsies from sacral nerves may also be obtained if indicated. If by cryostat sectioning and histologic examination these biopsies are negative, the amputation may proceed.

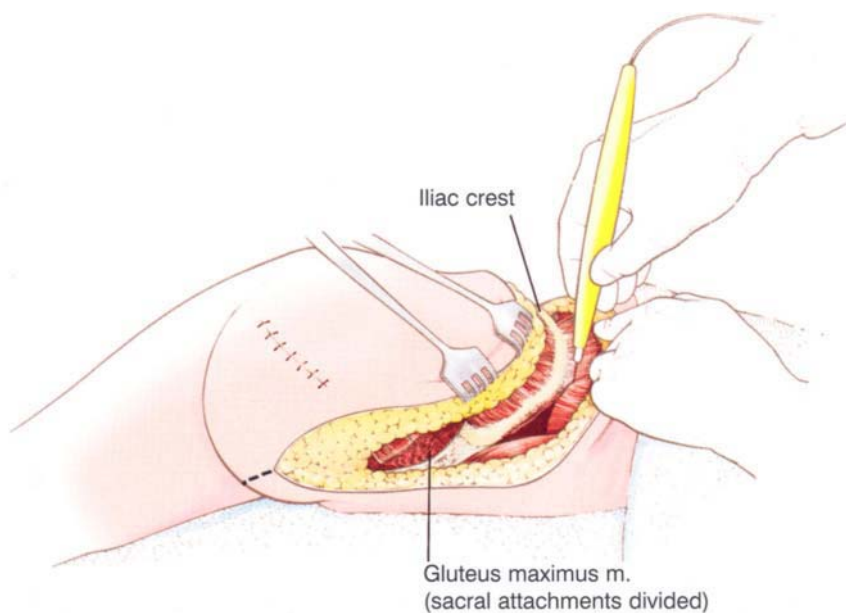


Figure 19.7 Release of back muscles from the iliac crest. Abdominal and back muscles that arise on the sacrum and the iliac crest are incised in the plane of attachment of muscle to bone to minimize blood loss. The muscles to be severed include the external oblique, erector spinae, latissimus dorsi, and quadratus lumborum.

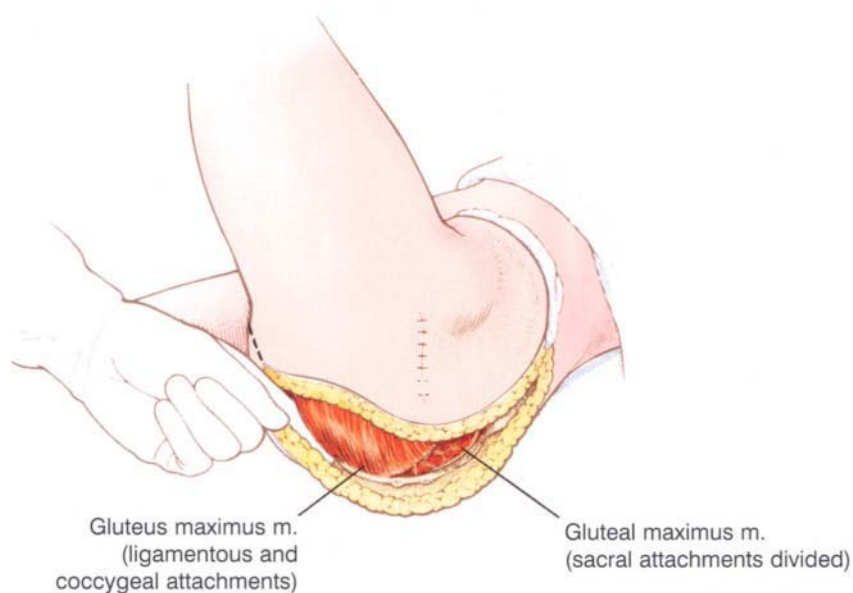


Figure 19.8 Posterior dissection in the ischiorectal space. The extremity is flexed at the hip to place the tissues in the area of the gluteal crease under tension. The perianal incision is extended toward the pubic tubercle along the gluteal crease. The deep dissection is continued lateral to the rectum into the ischiorectal fossa. The remaining origins of the gluteus maximus muscle are now severed from the coccyx and sacrotuberous ligament.

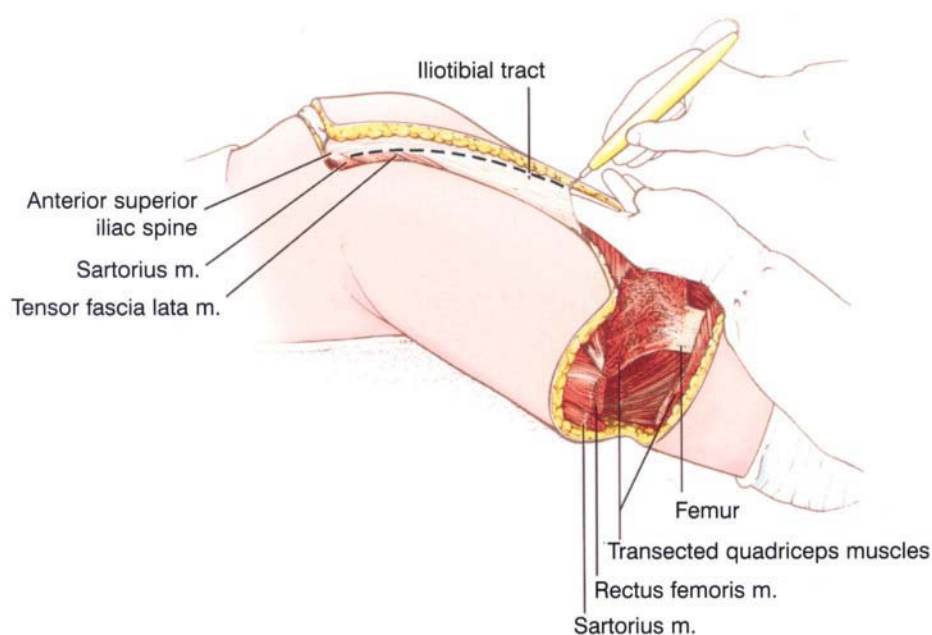


Figure 19.9 Lateral incision of the myocutaneous flap. The surgeon now moves from the posterior to the anterior aspect of the patient. The anterior incision at the junction of the middle and lower thirds of the thigh is made and continued down to the femur, transecting the entire quadriceps muscle. Laterally, this incision is continued superiorly toward the greater trochanter to the anterior superior iliac spine, the tensor fascia lata muscle is separated from its investing fascia so that it is included with the specimen.

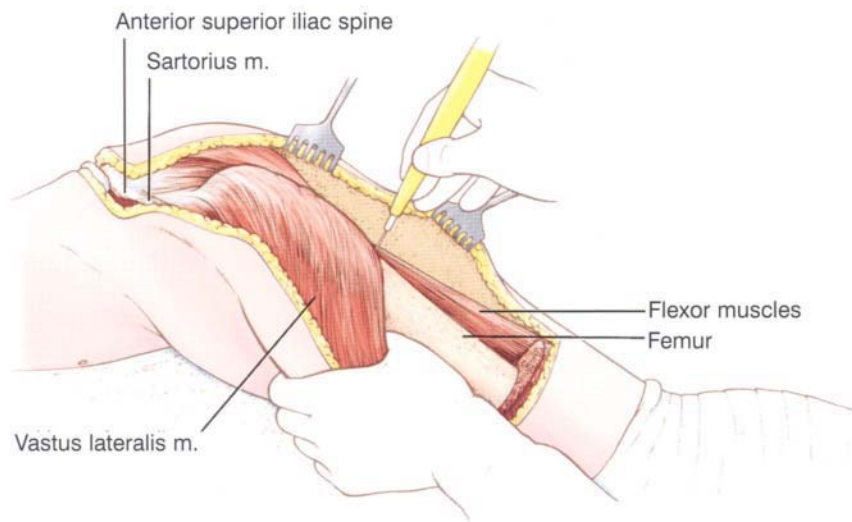


Figure 19.10 Release of the vastus lateralis from the femur. The fascial covering of the vastus lateralis of the quadriceps femoris muscle is dissected free of the flexor muscles and traced to its insertion on the femur. Then the vastus lateralis is severed from the femur using electrocautery. In performing the dissection from this point on, care must be taken not to separate muscle bundles of the myocutaneous flap from the overlying skin and subcutaneous tissue.

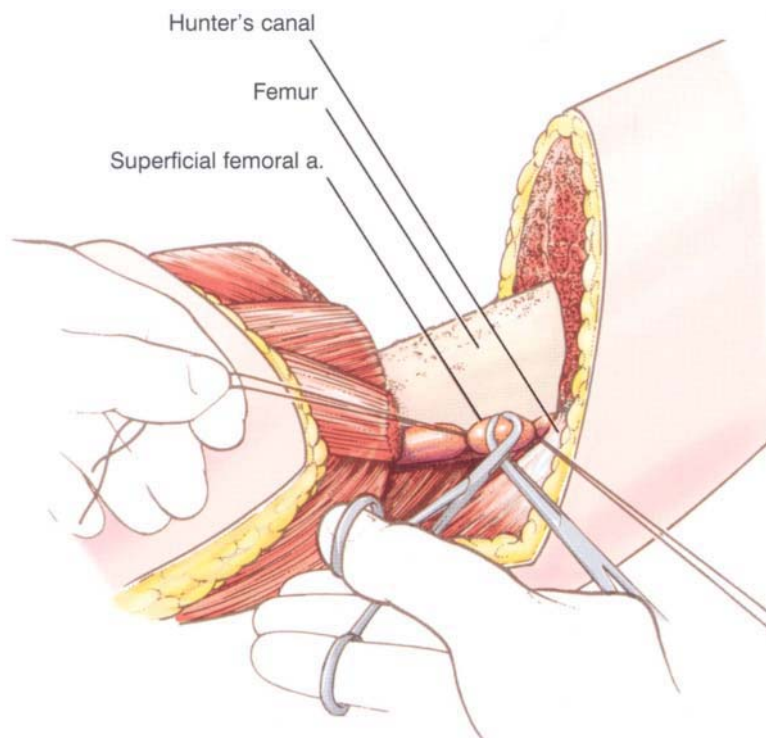


Figure 19.11 Transection of superficial femoral artery. The medial skin incision is from the area of Hunter's canal to the pubic tubercle. The superficial femoral vessels are located at their point of entry into the abductor muscles, and are ligated and divided at this level. These vessels course along the deep margin of the myocutaneous flap, and in the subsequent dissection they are traced superiorly to the inguinal ligament. Multiple small branches from the superficial femoral vessels to the abductor muscles must be clamped, divided, and ligated.

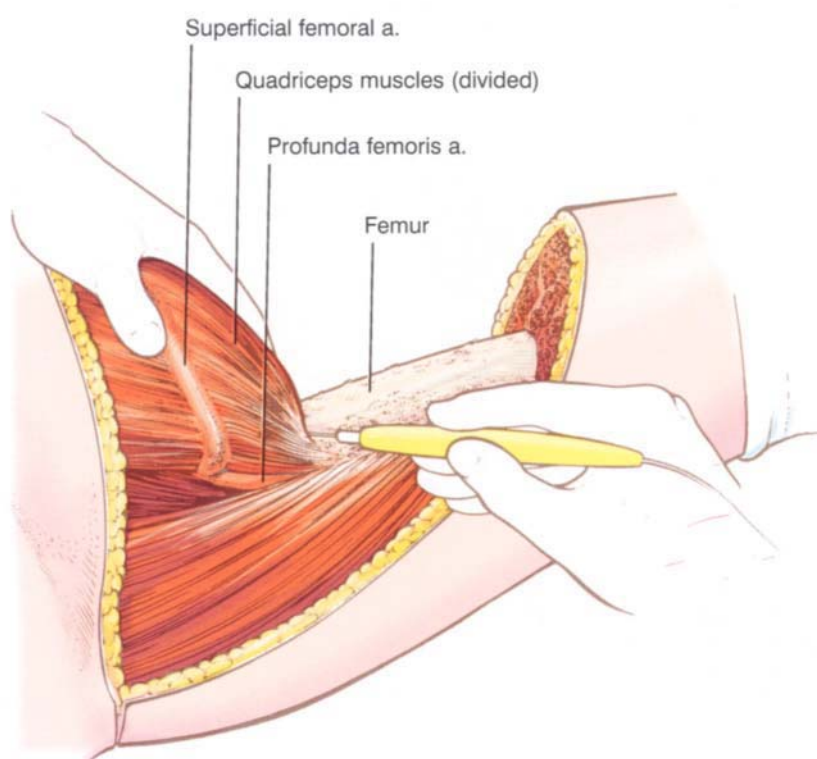


Figure 19.12 Release of the quadriceps muscle from the femur. Vigorous upward traction on the myocutaneous flap allows the origins of the vastus intermedius and the vastus medialis to be severed from the femur. As the release of the myocutaneous flap continues up toward the pelvis, the profunda femoris vessels are identified. These vessels are ligated and divided at their origin from the common femoral artery.

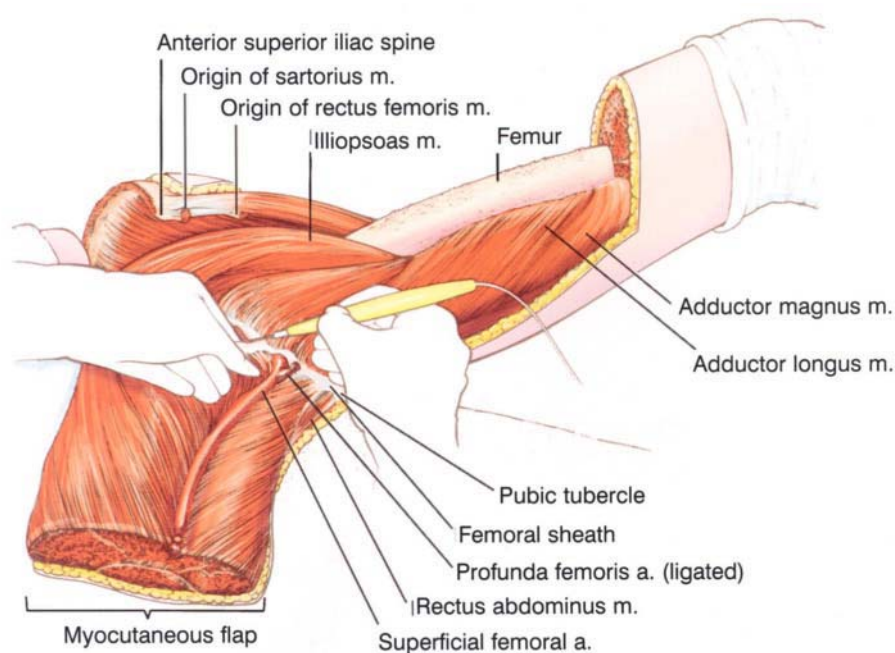


Figure 19.13 Release of the myocutaneous flap from the pelvis. The myocutaneous flap is freed from its pelvic attachments by the following procedure: the abdominal muscles and fascia are severed from the iliac crest; the sartorius muscle is transected at its origin on the anterior superior iliac spine; the rectus femoris is transected at its origin on the anterior inferior iliac spine; the femoral sheath overlying the hip joint is divided; and the left rectus abdominus muscle is released from the pubic bone. By retracting the myocutaneous flap medially, full access to the pelvis is achieved. Blunt dissection along the femoral nerve allows rapid dissection into the pelvis to expose the vessels and nerves to be transected in the subsequent phases of the procedure.

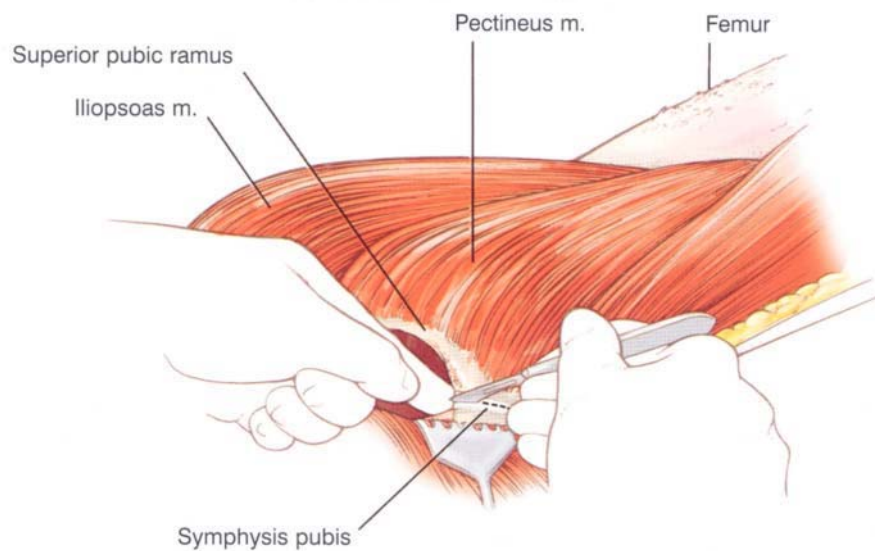


Figure 19.14 Division of the symphysis pubis. To divide the symphysis pubis, the bladder and urethra are protected and a scalpel is used to locate and divide the cartilaginous joint.

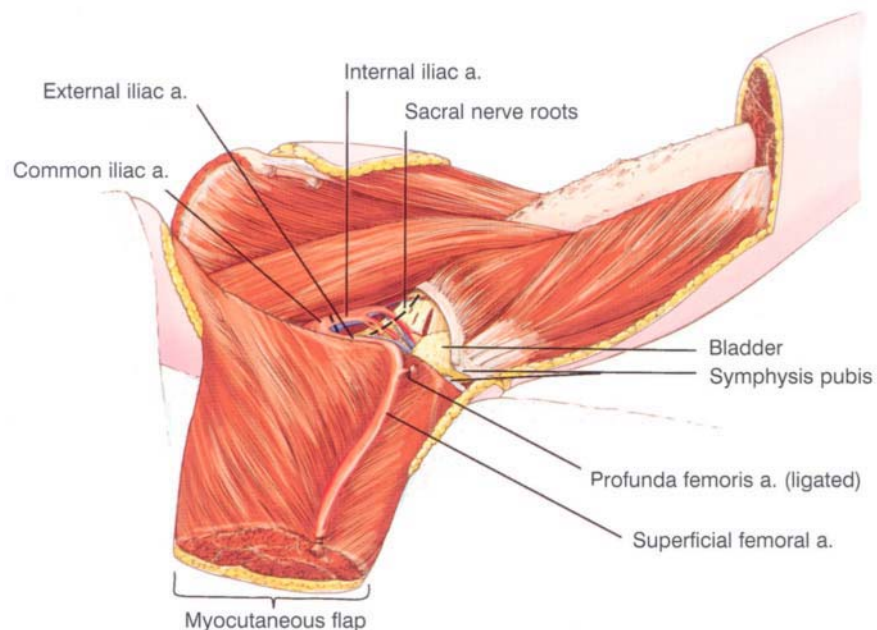


Figure 19.15 Transection of internal iliac vessels and branches. The internal iliac artery and vein are divided at their point of origin from the common iliac vessels. Multiple visceral branches of the internal iliac vessels are divided in their course superficial to the sacral nerve roots. Strong medial traction on the viscera will help expose these vessels. When this phase of the dissection is completed, the nerve roots should be clearly visualized throughout their course in the pelvis.

It should be noted that the common iliac lymph nodes remain with the patient in this procedure, in contrast to a standard hemipelvectomy, in which they are removed.

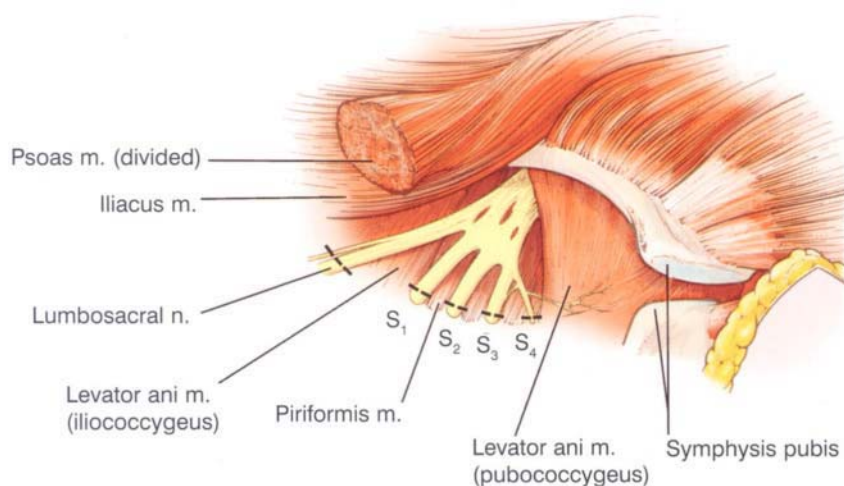


Figure 19.16 Division of the psoas muscle and nerve roots. The psoas muscle is divided near its junction with the iliacus muscle. The obturator nerve deep to the muscle is also divided. Care is taken to preserve the femoral nerve coursing into the myocutaneous flap. The lumbosacral and sacral nerve roots are ligated and divided close to the ventral sacral foramina.

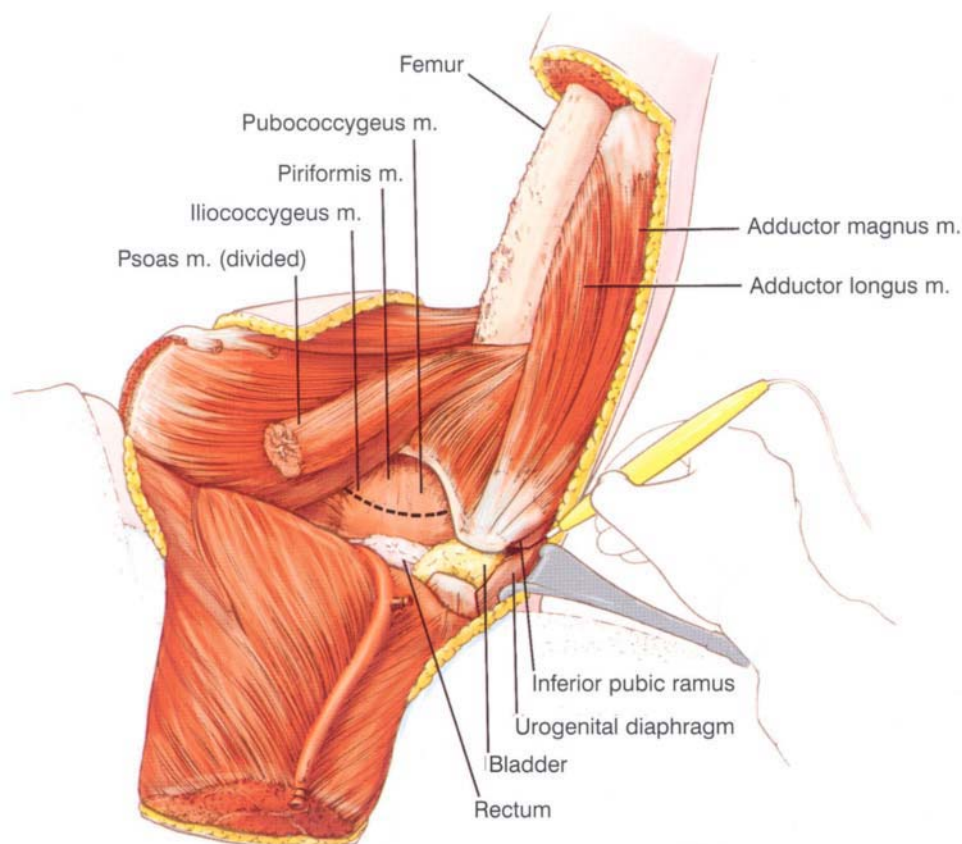


Figure 19.17 Division of the pelvic diaphragm. The leg is elevated to place under tension the individual muscles that constitute the pelvic diaphragm. Take care to protect the urethra, bladder, and rectum. The urogenital diaphragm, levator and piriformis muscles are divided. These muscles are transected near their pelvic attachments.

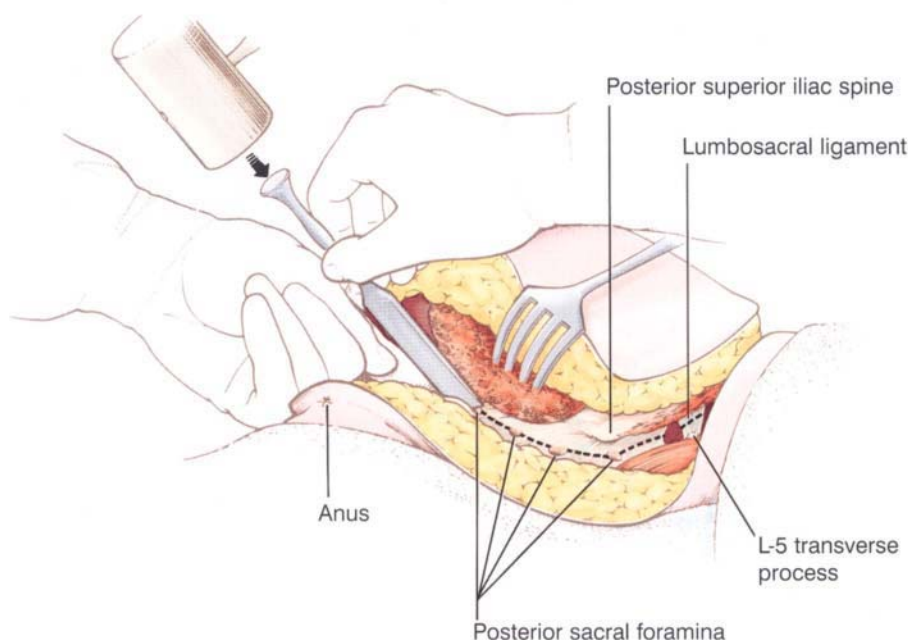


Figure 19.18 Division of the sacrum. The surgeon should again change orientation and move back to the posterior aspect of the patient. Using an osteotome and commencing at the tip of the coccyx, the coccyx and sacrum are divided in a plane that bisects the sacral foramina. Initially, the course of the osteotome should parallel the midsacral spines. The surgeon, being posterior to the patient, reaches around the coccyx with the left hand to locate the S-5 neural foramina from within the sacrum. This is at the junction of the sacrum and the coccyx. By holding the osteotome with the right hand, the direction for bone transection can be precisely determined. The assistant drives the osteotome through the bone with the mallet. At the upper portion of the sacrum, care must be taken not to fracture inadvertently through the bone. The lumbosacral ligament is divided to release the specimen.

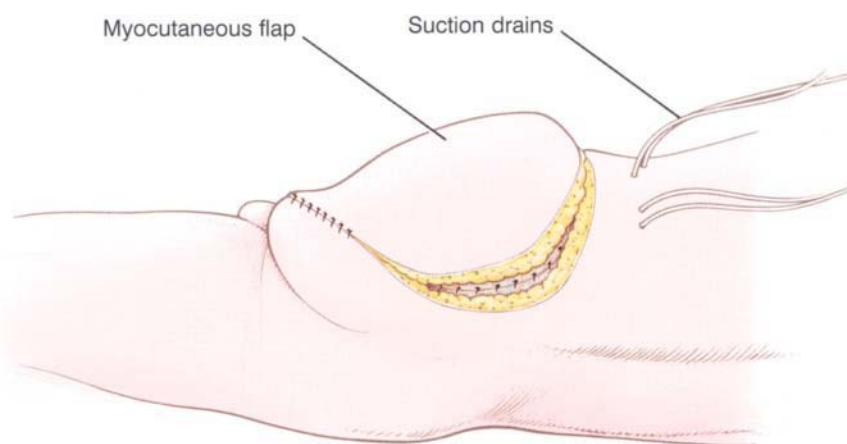


Figure 19.19 Closure. The operative site and myocutaneous flap are copiously irrigated and bleeding points are secured. The myocutaneous flap is folded posteriorly into the operative defect over two sets of suction drains. The fascia of the quadriceps femoris is sutured to the musculature of the anterior abdominal wall, to the back muscle, to the sacrum, and to the muscles of the pelvic diaphragm. The skin is closed with interrupted sutures.

If the patient is hemodynamically stable, ambulation may begin on the first postoperative day. The Foley catheter is removed at 1 week, and the suction drains are removed when the serous drainage is substantially reduced.

5. Ligation of profunda femoris.
6. Osteotomy of pubic symphysis and sacroiliac joint (or sacral alar).
7. Division of pelvic floor muscles.
8. Closure via flap rotation.

DISCUSSION

Patients with extensive soft-tissue sarcomas in the buttock, or patients with osteosarcoma of the pelvis extending posteriorly, have previously been thought incurable by amputation. Hemipelvectomy procedures formerly described required a flap of buttock skin to cover the surgical defect. Anterior flap hemipelvectomy allows sacrifice of the entire buttock and all the overlying skin and soft tissue to the midline. Even patients who have a tumor-contaminated buttock to the midline may have a potentially curative procedure.^{10,11}

If at all possible, tumors in this area, especially those of low histologic grade, should be treated with an excision of the gluteus maximus muscle (buttockectomy). However, if tumor extends through the gluteus maximus muscle to involve the gluteus medius or minimus, if tumor encases the sciatic nerve or if tumor is directly adjacent to the pelvic bones, a radical amputation utilizing an anterior myocutaneous flap is indicated.

Early postoperative complications with this procedure have not occurred to date. The serious problem of skin flap ischemia seen in nearly one-quarter of patients undergoing a standard posterior flap hemipelvectomy

has not been observed. The numerous muscular branches of the superficial femoral vessels to the quadriceps mechanism provide excellent blood supply to the preserved quadriceps muscles and to overlying skin and subcutaneous tissue. Care should be taken during the dissection not to shear overlying skin and subcutaneous tissue from the muscle mass; if this occurs, skin blood supply will be compromised.

The potential for rehabilitation with this procedure is excellent. The patients who are free of disease use a prosthesis regularly. Patients walk with the prosthesis without the use of crutches or cane. The large mass of quadriceps muscle provides a cushion of viable tissue on the sacrum on which a prosthesis may comfortably rest without traumatizing the overlying skin. [Figure 19.2E](#) shows the tissue mass created by the transplanted muscle that can be used to bear the weight required with use of a prosthesis.

The most bothersome long-term postoperative problem with this procedure (as with a standard hemipelvectomy) is phantom limb pain. Approximately 20% of patients currently surviving have severe phantom limb pain requiring narcotic analgesics on a daily basis. However, this incidence of phantom limb pain is not noticeably different from that seen with standard hemipelvectomy.

Occasionally, tumor tissue or heavily irradiated skin overlying the superficial femoral artery may require sacrifice of the skin pedicle. In this instance the island myocutaneous flap should be utilized.

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Posterior Flap Hemipelvectomy

Martin Malawer and Robert Henshaw

OVERVIEW

In spite of increasingly effective chemotherapy and advances in limb-sparing surgery around the pelvis and hip (see Chapter 10), hindquarter amputation (hemipelvectomy) often remains the optimal surgical treatment for primary tumors of the upper thigh, hip, or pelvis. Hemipelvectomy may also be life-saving for patients with massive pelvic trauma or uncontrollable sepsis of the lower extremity, and it can provide significant palliation of uncontrollable metastatic lesions of the extremity.¹⁻³ An intimate knowledge of the pelvic anatomy ([Figures 20.1A,B](#)) and a systematic approach to the surgical procedure are required to minimize the intraoperative and postoperative morbidity associated with this demanding procedure.

The patient is placed in a modified semi-supine position. Incision of the abdominal wall and retroperitoneal dissection of the iliac vessels are performed first. The common iliac, external iliac, or internal iliac (hypogastric) vessels are selectively ligated according to the type of hemipelvectomy to be performed. Exposure of the pubis, bladder neck, and urethra permits sectioning of the symphysis pubis. The iliac wing, sacroiliac joint, or sacrum is then exposed and divided to complete the amputation. Division of the lumbosacral plexus at the level of the sacrum or pelvis is accomplished at the same time. A fasciocutaneous or a myocutaneous flap (involving the gluteus maximus for posterior flaps or the anterior compartment of the thigh for anterior flaps) is then completed. Flexion and adduction/abduction of the hip then allows the surgeon to divide the muscles and ligaments of the pelvic floor and complete the amputation. The wound is closed by rotating and suturing the prepared myocutaneous flap to the abdominal wall and flank. Maximizing the patient's functional outcome requires the combined skills of an experienced multidisciplinary team of physical, occupational, and rehabilitative therapists.

INTRODUCTION

Early descriptions of the surgical technique of hemipelvectomy emphasized the importance of careful selection of patients and immediate replacement of blood loss.⁴⁻¹⁸ Other, later technical descriptions of this procedure have been published.¹⁹⁻²⁵ Recent reports of series of hemipelvectomy patients have shown this procedure to have a low mortality rate and to offer an acceptable survival in carefully selected patients.^{25,26} Quality-of-life studies suggest that long-term morbidity in patients who have undergone this radical amputation is not greater than that experienced by patients who have undergone other cancer treatments.²⁷

CLASSIFICATION

Current terminology for major amputations through the pelvis is overly simplistic and consequently confusing. The terms "hindquarter" amputation and "hemipelvectomy" are often used interchangeably to refer to any amputation performed through the pelvis. Older terms used to describe this same procedure include interpelviabdominal⁴ or interinnomino-abdominal⁵ amputation to describe this same procedure. The

advent of limb-sparing pelvic resections has necessitated a distinction between internal and external hemipelvectomy, depending on whether preservation of the ipsilateral limb is performed. Confusion caused by the term "internal hemipelvectomy" can be avoided by use of a standardized classification for pelvic resection (see Chapter 26).

Sugarbaker^{28,29} and others³⁰⁻³⁶ have shown the utility of a myocutaneous pedicle flap based upon the femoral vessels and anterior compartment of the thigh for closure of the wound in patients with tumor involving the posterior buttock structures. This procedure has been termed an "anterior flap hemipelvectomy", to distinguish it from the more common "posterior flap hemipelvectomy". Anterior flap hemipelvectomy is indicated for tumors that involve the buttock and for selected patients in whom a well-vascularized flap is required for coverage.

There are subtypes of the posterior flap hemipelvectomy (Figure 20.1C). The term "classic hemipelvectomy" is used to refer to amputation of the pelvic ring via disarticulation of the pubic symphysis and the sacroiliac joint (SI), division of the common iliac vessels, and closure with a posterior fasciocutaneous flap. Classic hemipelvectomy is typically necessary for large

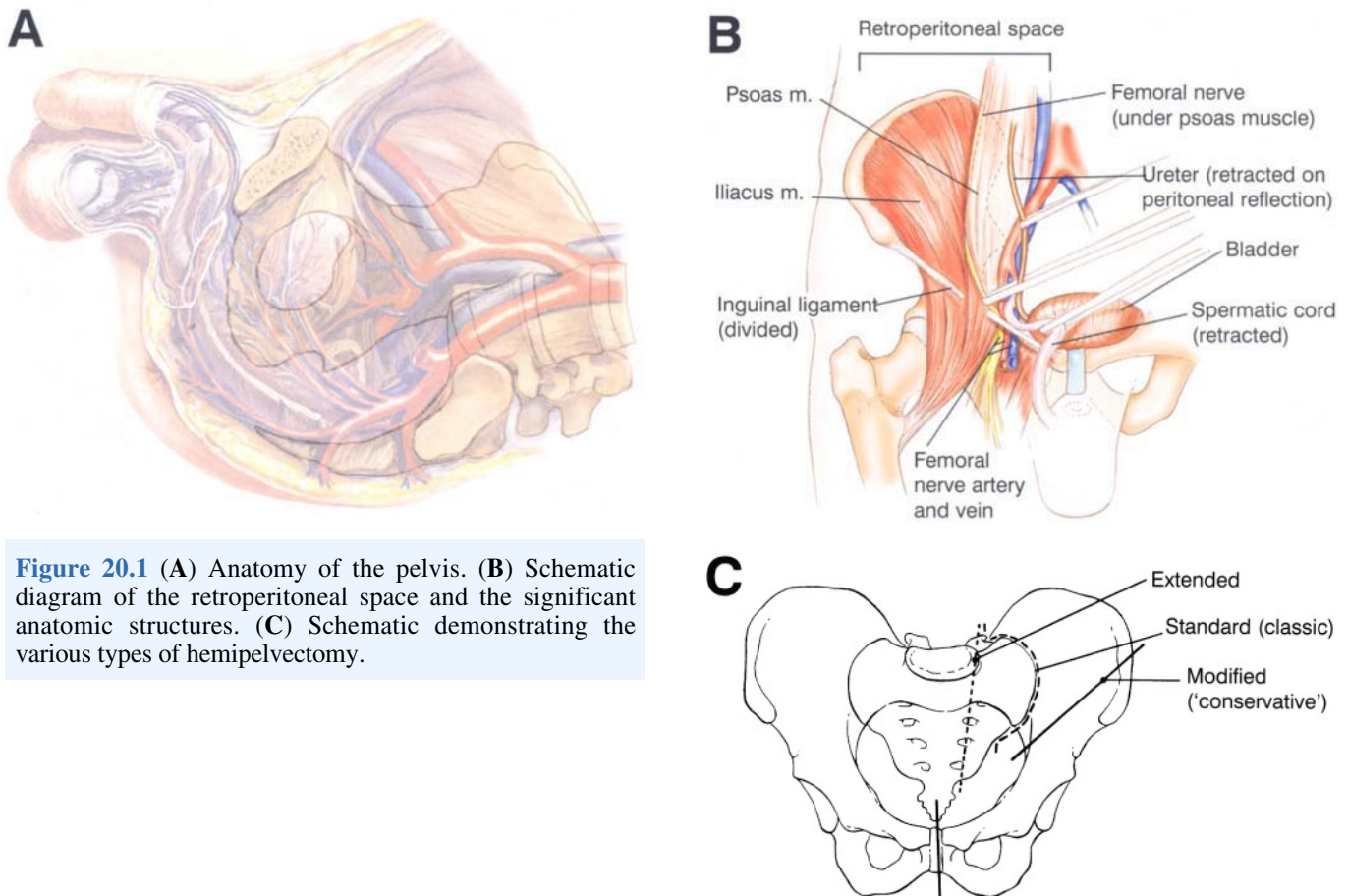


Figure 20.1 (A) Anatomy of the pelvis. (B) Schematic diagram of the retroperitoneal space and the significant anatomic structures. (C) Schematic demonstrating the various types of hemipelvectomy.

tumors that arise within the pelvis. "Modified hemipelvectomy" refers to a procedure that preserves the hypogastric (internal iliac) vessels and the inferior gluteal vessels supplying the gluteus maximus, permitting creation of a vascularized myocutaneous posterior flap for wound closure. This term also describes any and all variations from the classic operation, including resection through the iliac wing or contralateral pubic rami. Modified hemipelvectomy is most commonly performed for tumors involving the thigh and/or hip, when a limb-sparing alternative is contraindicated. "Extended hemipelvectomy" refers to a resection of the hemipelvis through the sacral alar and neural foramina, thereby extending the margin for tumors that approach or involve the SI joint.

Regardless of the type of flap created for closure, the term "compound hemipelvectomy" is used to describe resection of contiguous visceral structures such as bladder, rectum, prostate, or uterus. (Patients suspected of having tumor extending into viscera, or an extremely large tumor filling the pelvic fossa, can be approached through an intraperitoneal incision.)

INDICATIONS

The advent of limb-sparing procedures combined with effective chemotherapy and/or radiation therapy has greatly reduced the need to perform radical amputations of the lower extremity. Increasing experience with less radical resections of the pelvis (see Chapter 10) and new techniques of reconstruction following removal of the acetabulum and hip joint have further reduced the number of patients requiring a hemipelvectomy. The adoption of vascular grafts and advances in rotational flaps and microvascular free flaps extended the indications for limb-sparing surgery. Finally, recognition that deficits from femoral or sciatic nerve resection may be overcome by patient education and bracing of the knee or ankle has further increased the number of patients that can undergo a limb-sparing procedure. Nonetheless, some patients will still require a hemipelvectomy (Figures 20.2–20.4).

Indications for Hemipelvectomy

Unresponsive Sarcomas Involving Multiple Compartments

The most common indication for hemipelvectomy is a nonmetastatic sarcoma that fails to respond to neoadjuvant chemotherapy and/or radiation. In addition, patients with extremely large sarcomas (Figure 20.5) involving multiple compartments of the thigh may require an immediate amputation to avoid tumor fungation, hemorrhage, and secondary infection. In each case the type of hemipelvectomy performed in these

circumstances is dictated by the anatomic location of the tumor and the expected defect to be created by the resection. For example, a posterior tumor involving the buttock and sciatic nerve that cannot be resected by a buttockectomy can be removed and closed with a vascularized pedicle anterior flap hemipelvectomy.



Figure 20.2 CT scan showing a large secondary chondrosarcoma (arrow) arising from the left proximal femur in a patient with multiple hereditary osteochondromatosis. Note the gluteus maximus (g) was completely free of tumor. This patient was a perfect candidate for a modified posterior flap hemipelvectomy.

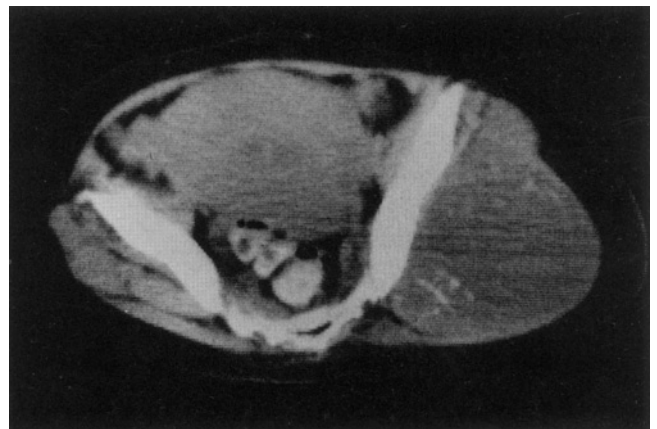


Figure 20.3 CT scan showing a large chondrosarcoma arising from the iliac wing approaching the sacroiliac joint involving the gluteus maximus muscles. This patient is not a candidate for a posterior flap hemipelvectomy and required an anterior flap hemipelvectomy for adequate margins to be obtained posteriorly.

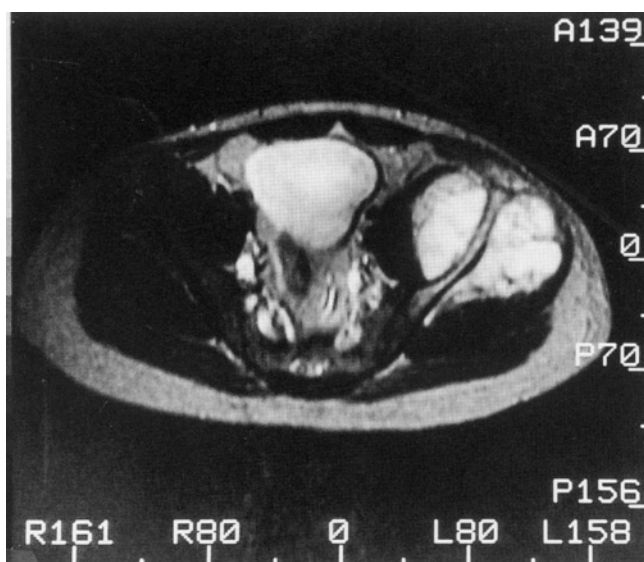


Figure 20.4: MRI scan of an osteosarcoma stage IIB involving the entire wing of the ilium with extension to the superacetabular area. This patient underwent a classical hemipelvectomy.

Contamination of Surrounding Structures

Patients with extensive contamination of compartments from inappropriately placed biopsies and/or from unplanned intralesional resections of sarcomas around the pelvis, hip, and proximal thigh are candidates for hemipelvectomy. In addition, pathologic fractures of the proximal femur often contaminate unexpectedly large volumes of tissue. Traditionally, such fractures have been treated with hemipelvectomy, although some institutions now attempt limb-sparing procedures following aggressive preoperative (neo-adjuvant) treatment and spica immobilization.

Nonviable Extremity Precluding Limb Salvage

Elderly patients with significant peripheral vascular disease, or patients with fungating, infected sarcomas that preclude limb-sparing surgery, may be candidates for hemipelvectomy (Figure 20.6). Conversely, very young and skeletally immature children with primary sarcomas who are not suitable candidates for limb-sparing procedures because of the inevitable problem of limb-length discrepancy may be treated with hemipelvectomy. Typically, the youngest patients adapt most completely to their missing limb and lead extremely active lives. Psychological counseling for the parents and family is essential under such circumstances.



Figure 20.5 (A) CT scan of an extremely large leiomyosarcoma of the pelvis and adductor region. (B) Tumor destruction of the pelvic floor as well as the symphysis pubis and involvement of the hip joint.

Failure of Previous Resection

Hemipelvectomy is indicated as a final salvage procedure for patients with local recurrence in the thigh or buttock following aggressive surgical and medical treatment. Careful patient evaluation is necessary to rule out the presence of metastatic disease in such cases. Hemipelvectomy may also be required for the control of infection following limb-sparing procedures around the hip and pelvis.

Palliation

The use of radical amputation for palliation of patients with metastatic disease is rare.^{37–39} Palliative indications



Figure 20.6 Clinical photograph of a patient who had undergone a hip disarticulation after a failed aortal–femoral bypass graft with secondary infection and flap necrosis. This is one of the most common clinical indications for a hemipelvectomy. The patients with failed vascular grafts at a higher level are often septic at the time of surgery and require emergency surgery.

for hemipelvectomy include uncontrollable pain from tumor involvement of the lumbosacral plexus, sciatic, and femoral nerves. Patients with uncontrollable local disease from metastatic carcinoma who have failed all conventional treatments, including radiation and chemotherapy, may also benefit from amputation. Realistic expectations and psychological support for the patient and family are essential in such cases.

Nononcologic Indications

Modified or anterior flap hemipelvectomy may be required for uncontrolled decubiti and osteomyelitis of the hip and pelvis in patients with long-standing paralytic conditions.⁹ Both function and emotional

well-being often improve rapidly after the source of chronic sepsis has been surgically removed. For patients with partial pelvic amputation and open hemorrhaging fractures of the pelvis, emergency hemipelvectomy may be life-saving.⁴⁰ In both circumstances, oncologic margins are not required, making the surgery easier to perform.

CLINICAL CONSIDERATIONS

Minimizing of the morbidity and mortality associated with hemipelvectomy requires careful physical and psychological preparation of the patient. Patients receiving preoperative chemotherapy or radiation therapy require time to recover from their neutropenia and anemia. Use of supportive growth factors such as erythropoietin and GCSF may be of significant benefit. Replacement of red cell mass by blood transfusion and correction of bleeding abnormalities are essential to reduce the risk of intraoperative mortality. In addition, patients with poor nutrition secondary to disease and the nausea and vomiting induced by chemotherapy may require hyperalimentation before and after surgery to reduce problems with wound healing.

To reduce the risk of postoperative infection, bowel preparation should be performed for all patients. Perioperative antibiotic coverage for aerobic skin flora and anaerobic bowel flora is required. Postoperative care to prevent hematomas and seromas includes the use of large-bore suction drains and pressure dressings using Ace wraps. A Foley catheter and a nasogastric tube are used to prevent abdominal distension that, in turn, reduces pressure on the skin closure. Skin sutures or staples should be retained for 3–4 weeks to minimize the risk of wound dehiscence.

Patients undergoing hemipelvectomy face a unique combination of psychological stress related to the loss of limb and potential loss of life from the underlying disease. Ongoing psychological support for the patient and family is essential. Rehabilitation of the patient begins at the time of the staging studies. The entire health-care team must develop and maintain an honest relationship with the patient and the family and include them in the decision-making process. Trust and understanding can be enhanced by having the patient meet others who have undergone this procedure, and helping the patient accept the amputation and set realistic goals.

Although hemipelvectomy has traditionally been associated with extensive blood loss, strict adherence to the techniques described here can result in an estimated blood loss (EBL) of 500–2000 ml. Use of growth factors such as erythropoietin and nonhemologic plasma expanders has allowed us to perform this

amputation without blood transfusion on a Jehovah's Witness patient. Meyers *et al.* have also reported successful hemipelvectomy under these circumstances.⁴¹ However, for patients in whom the tumor encases or involves the major vessels, extensive bleeding should be anticipated. Extensive blood loss and replacement in excess of one to two times the patient's circulatory volume may create life-threatening coagulopathies and pulmonary complications.

Another serious postoperative complication is wound necrosis. Ligation of the common iliac vessels during a classic posterior flap hemipelvectomy deprives the flap of its major blood supply; 10–50% of patients may develop clinically significant ischemia. Pressure from prolonged laying or sitting on the flap may result in ischemic necrosis. Early identification of necrosis and surgical revision is recommended as being essential to minimize additional complications. Meticulous attention to preserving the fasciocutaneous vessels and a portion of the gluteus maximus can reduce the incidence of ischemic necrosis.

All patients undergoing hemipelvectomy have significant risk factors for infection, such as tumor-related catabolism, chronic malnutrition, and chemotherapy-induced anemia and neutropenia. As a result it is not surprising that infection may be seen in approximately 15% of patients. Additional factors that increase the risk of infection include immunosuppression from surgical stress, transfusions, and psychological depression. Steps to reduce the incidence of infection should include the use of preoperative bowel prepping, use of a purse-string suture to close the anus during surgery, broad-spectrum perioperative antibiotic coverage, and the use of large-bore closed suction drains to prevent retroperitoneal hematomas. Infection may significantly retard wound healing; aggressive surgical debridement and prolonged dressing changes are often necessary.

Intraoperative retraction of the peritoneum and use of postoperative narcotics contribute to the development of an ileus that may last for a week or more. Routine placement of a nasogastric tube and avoidance of oral feeding are required to prevent nausea, vomiting, aspiration, abdominal distension, and possible wound complications. Early intravenous nutritional supplementation should be considered.

Division of the sacral plexus may result in loss of innervation of the ipsilateral bladder and penis, resulting in bladder atony and impotence. These problems are often transient and often resolve within 1–3 months as the contralateral innervation becomes dominant. An indwelling Foley catheter should be maintained until the patient becomes mobile, and post-void residuals should be measured once the catheter is removed.

All amputees experience phantom limb sensation. Patient education, aggressive medical treatment, and rigorous physical rehabilitation play a role in minimizing the impact of these sensations. Injection and infusion of local anesthetics into the lumbosacral plexus and stumps of the sciatic and femoral nerves may significantly reduce actual pain and phantom sensation in the immediate postoperative period (see Chapter 24).

A prosthesis should be offered to all patients, even though all of them may not use it. If a segment of ilium has been preserved, a suspension belt may be used. Elderly and overweight patients may become wheelchair-dependent following this procedure because of the increased workload required to ambulate. Some children and adults find that a prosthesis slows their ability to ambulate with crutches. The prosthesis enables the wearer to stand for prolonged periods of time without supports and frees both hands for other activities (see [Figure 20.19](#), in Rehabilitation section of this Chapter).

UNIQUE ANATOMIC CONSIDERATIONS

The skeletal anatomy and contents of the pelvis are complex and difficult to visualize without direct experience. Major portions of the gastrointestinal tract, the urinary tract, the reproductive organs, and the neurovascular trunks to the extremities all coexist within the confines of the bony pelvis. Understanding the three-dimensional anatomy is essential to identifying and protecting these structures during a hemipelvectomy ([Figure 20.1](#)). It is also important to recognize that the normal anatomy may be distorted by the tumor. Reference to easily palpable and visual landmarks helps identify critical structures. The surgical approach to a hemipelvectomy is based upon sequential exposure and identification of these landmarks and structures.

Bony Anatomy

The basic pelvic bony anatomy is best thought of as a ring, running from the posterior sacrum to the anterior pubic symphysis. Major joints include the large, flat sacroiliac joints, the hip joints and the pubic symphysis. The hip joint is easily located by motion of the extremity, while the other joints are easily located and identified by palpation. Other easily palpable bony prominences include the iliac crest, the anterior superior iliac spine (ASIS), the ischial tuberosity, and the greater trochanter of the femur. These landmarks are essential in creating rational skin incisions during the procedure. Likewise, identification of internal bony landmarks helps localize adjacent structures. The

lumbosacral plexus is found by palpating the SI joint, the sciatic nerve and gluteal vessels are found under the sciatic notch, the urethra is found under the arch of the pubic symphysis.

Vascular Anatomy

Ligation of the correct pelvic vessels is crucial to a successful amputation. The importance of this fact is indicated by the classification scheme, in which the level of ligation determines the type of amputation to be performed. As the abdominal aorta and vena cava descend into the pelvis they bifurcate, creating the common iliac arteries and veins. This bifurcation typically occurs at L4, with the lower bifurcation occurring at S1. The left-sided aorta and the iliac and external iliac arteries remain anterior to the major veins throughout the pelvis. The internal iliac artery (hypogastric artery) bifurcates from the posterior surface of the common iliac artery as it travels down toward the sciatic notch. Tumor masses within the pelvis can distort this anatomy, making it mandatory to visualize and isolate each of the vessels prior to performing a ligation (see [Figure 20.1A](#)).

The internal iliac (hypogastric) vessels supply the pelvic floor, rectum, bladder, and prostate, as well as the gluteal muscles. Ligation of this vessel will not jeopardize the internal structures because of contralateral blood flow and rich anastomotic vessels; however, it will significantly devascularize the gluteus maximus muscle. Classic hemipelvectomy, in which these branches are divided, has a substantial rate of wound complications as a direct result.

Pelvic Viscera

In addition to the critical vascular structures, major organs of the gastrointestinal and genital–urinary tracts are present and exposed during a hemipelvectomy. These structures should be completely evaluated prior to surgery.

The bladder and urethra, and the prostate in males, are located above and under the pubic symphysis. Placement of a Foley catheter with a large inflated balloon makes these structures easier to palpate during surgery. Care must be taken not to injure the urethra during division of the symphysis. In addition, the venous plexus surrounding the prostate can be a significant source of bleeding that can be difficult to control even with good visualization of the organ. The ureters are at risk of injury as they cross over the iliac vessels, from lateral to medial. The peristaltic motion of the ureters helps to identify these structures.

In female patients, the ovaries, fallopian tubes, uterus, cervix, and vagina require identification and

protection. Care in taking a complete history of the patient will identify those women who have undergone hysterectomies. In women who have not undergone such surgery, these structures are found under and adjacent to the bladder. They can be easily and safely retracted out of the operative field.

The majority of the gastrointestinal tract is protected by the peritoneum and is gently retracted out of the operative field. Of particular concern is the sigmoid colon, which must be protected during left-sided amputations. The colon and rectum must also be identified and protected during the division of the sling muscles prior to completion of the amputation. Insertion of a rectal tube prior to surgery helps to identify both these structures and to decompress them. Because of the possibility of bacterial contamination from these structures, preoperative bowel preparation and the use of appropriate antibiotics is prudent.

PREOPERATIVE IMAGING/STAGING STUDIES

Complete imaging and staging of the patient are essential to proper patient selection and preoperative planning. Routine preoperative staging studies of the patient should include computed tomography (CT) scan of the chest and total body bone scan to detect metastatic disease. Images of the liver and abdomen may be indicated for patients with certain tumors, such as myxoid liposarcomas, that can present with unusual sites of metastases.

Standard X-Rays

X-rays remain the gold standard for the detection and diagnosis of bone sarcomas. Evaluation of patients with suspected pelvic and hip/thigh tumors should always include a standard anteroposterior (AP) pelvis view that extends from the top of the iliac crests to below the pubic symphysis. Additional views of the pelvis may be helpful, including iliac and obturator oblique views described by Judet;⁴² as well as inlet and outlet views. Given the complexity of pelvic anatomy, cross-sectional images are vital ([Figure 20.7](#)).

CT and MRI

CT and magnetic resonance imaging (MRI) both provide the ability to image pelvic anatomy in cross-sectional planes; MRI provides better images in the sagittal and coronal planes. Use of oral, IV and rectal contrast media can greatly facilitate the ability of CT scan to image visceral organs of the pelvis. CT is extremely useful in the evaluation of the sacroiliac joint, the sciatic notch, and the symphysis pubis. MRI often provides a better image of the soft tissue and

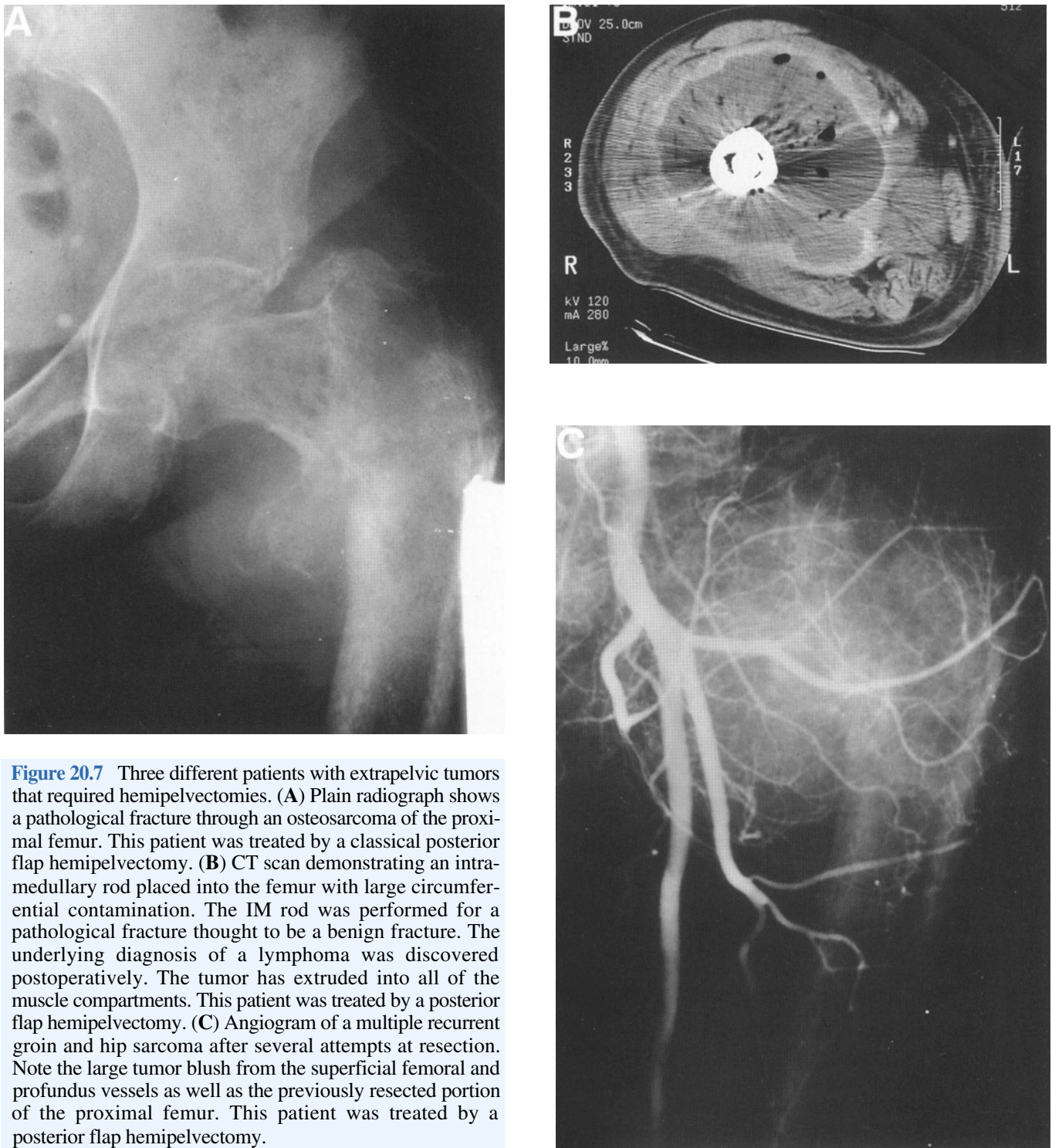


Figure 20.7 Three different patients with extrapelvic tumors that required hemipelvectomies. (A) Plain radiograph shows a pathological fracture through an osteosarcoma of the proximal femur. This patient was treated by a classical posterior flap hemipelvectomy. (B) CT scan demonstrating an intramedullary rod placed into the femur with large circumferential contamination. The IM rod was performed for a pathological fracture thought to be a benign fracture. The underlying diagnosis of a lymphoma was discovered postoperatively. The tumor has extruded into all of the muscle compartments. This patient was treated by a posterior flap hemipelvectomy. (C) Angiogram of a multiple recurrent groin and hip sarcoma after several attempts at resection. Note the large tumor blush from the superficial femoral and profundus vessels as well as the previously resected portion of the proximal femur. This patient was treated by a posterior flap hemipelvectomy.

intramedullary extent of sarcoma (see Figure 20.4). The retroperitoneal lymph nodes can be evaluated with either technique. Because of the complementary nature of the information provided by these scans, a complete evaluation of a given patient may require the use of both imaging modalities (Figures 20.7B and 20.8).

Angiography

Preoperative angiography of the pelvis is extremely useful in delineating the relationship of the iliac branches to the tumor. Older patients undergoing anterior flap hemipelvectomy may have silent

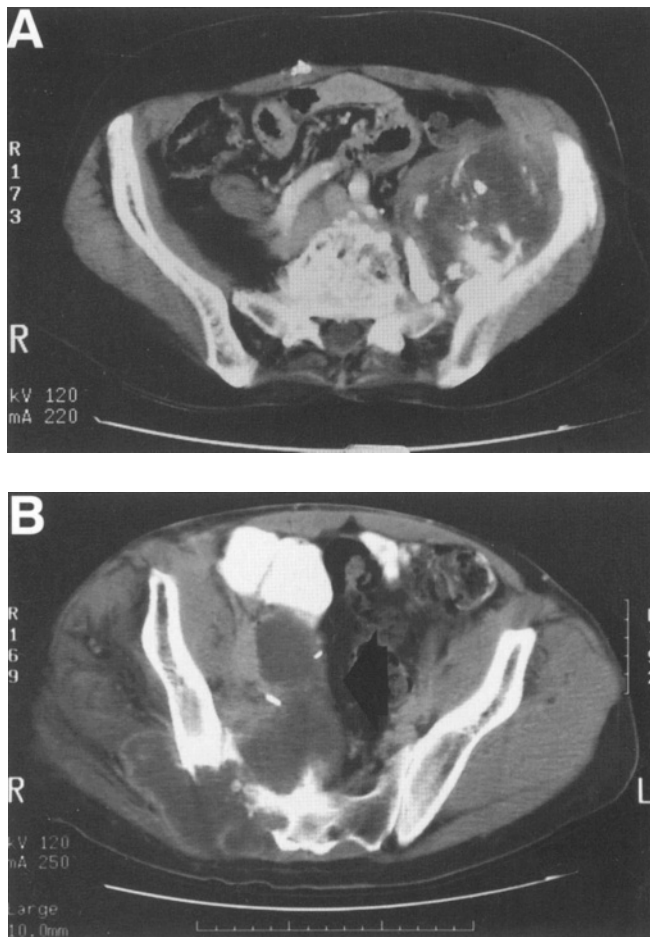


Figure 20.8 CT scans of two different patients demonstrating the inoperability of large sarcomas around the pelvis that may involve the sacrum. (A) CT scan of a radiation-induced osteosarcoma of the left ilium that crosses the sacroiliac joint and involves S1 and L5. Note the large intrapelvic component with S-I joint involvement and destruction. (B) CT scan of an extremely large chondrosarcoma arising from the right posterior wing of the ilium and sacroiliac joint with marked involvement of the sacrum with a huge intrapelvic extension crossing the midline (arrow). Note the hemoclips that denoted the area of an open biopsy and exploration. There is marked tumor necrosis following postoperative radiation therapy. This patient was inoperable due to the local extension of the tumor intrapelvically and intraspinally.

atherosclerotic disease of the femoral vessels that could jeopardize the success of the flap. For patients in whom a modified hemipelvectomy is considered, angiography reveals the level of the common iliac bifurcation. Patients undergoing palliative amputation may benefit from preoperative embolization to reduce intraoperative bleeding (see Figure 20.7C).

Venography and Other Tests

Complete evaluation of the visceral structures of the pelvis may require additional studies. Dedicated radiographic evaluation using contrast materials of the colon, rectum, bladder, urethra, and uterus is useful if tumor involvement is suspected. Direct visual inspection via sigmoidoscopy and cystoscopy may be essential in selected patients. Pelvic venography should be performed if there is any clinical suspicion of venous obstruction, i.e. distal edema. Venous tumor thrombi often occur with large pelvic chondrosarcomas. Tumor thrombi should be removed during the operative procedure.

SURGICAL GUIDELINES

The classical posterior flap hemipelvectomy can be visualized as consisting of five major surgical components.

1. *Anterior retroperitoneal approach through the ilioinguinal incision.* Through this incision the retroperitoneal space is explored. The iliac arteries or hypogastric vessels are ligated and transected, the psoas muscle and the femoral nerve are transected, and the abdominal wall is released from the iliac crest from the symphysis pubis to the posterior superior iliac spine. *Note:* all structures are transected or mobilized anteriorly before proceeding on to the next steps of the operative procedure.
2. *Perineal incision.* The second major step is the perineal incision. This incision extends from the symphysis pubis down to the ischium along the inferior pubic ramus. The ischiorectal space is exposed along the inferior pubic ramus to the symphysis pubis. The symphysis pubis is disarticulated. The bladder is protected with a large malleable. The urethra is protected similarly.
3. *Posterior flap retrogluteal area exploration.* The third component of the procedure is the posterior fasciocutaneous or subcutaneous flap that is mobilized along the iliotibial band and the greater trochanter towards the sacroiliac joint. A classical hemipelvectomy involves the removal of all gluteal structures and only the subcutaneous flap remains.
4. *Detachment of pelvic floor musculature.* This maneuver is performed with the hip abducted and flexed, with the surgeon standing between the two extremities, facing the pelvis. While the assistant abducts the extremity, the pelvic floor musculature is stretched and ligated through Kelly clamps, beginning at the pubic ramus and ending at the sacroiliac joint.
5. *Completion of the amputation with sacroiliac disarticulation.* The amputation is completed by transecting

the sacroiliac joint with a large osteotome while retracting the peritoneal contents and avoiding the previously transected iliac vessels.

Closure of the flap is then performed over large 28-gauge chest tubes with suction drainage. Marcaine epineural catheters are utilized for continuous pain relief postoperatively. Two catheters are used: one is placed into the lumbosacral plexus and the other is inserted into the femoral nerve.

The following illustrations demonstrate the surgical technique for performing a posterior flap hemipelvectomy.

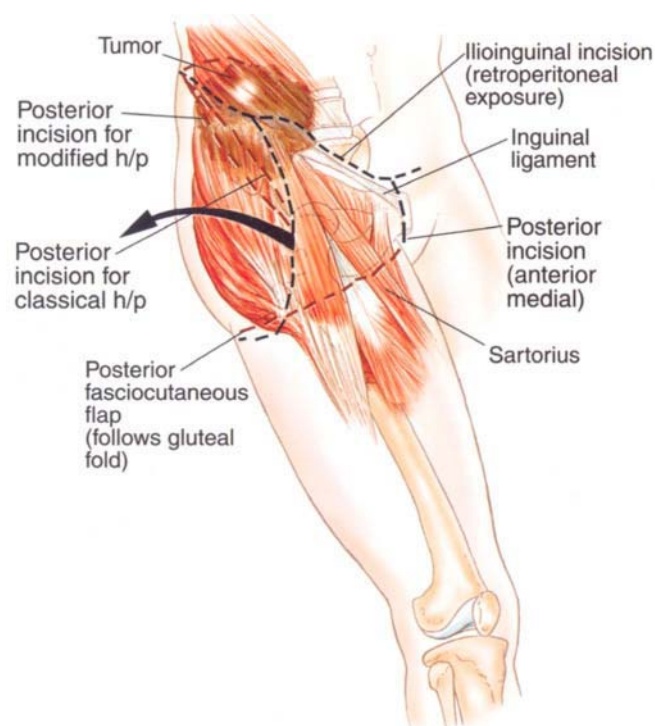


Figure 20.9 Incision and position. The patient is placed on the operating table in a semisupine position. This permits anterior retroperitoneal surgery under an anterior approach. The perineal incision can then be performed with the hip abducted and flexed. The posterior gluteal incision is performed with the patient in a semilateral position with the table rotated to the opposite side. This position is preferred in contrast to the typical lateral position frequently used by other authors. The incision consists of three components: anterior ilioinguinal approach extending from the symphysis pubis along the ilioinguinal ligament and then along the iliac crest to the posterior superior sacroiliac joint. The perineal incision is made from the symphysis pubis and along the inferior pubic ramus to the ischium. The third part of the incision is the posterior incision that is made from the mid-portion of the anterior incision coursing down toward the greater trochanter and to the skinfold of the gluteus maximus muscle. This incision crosses the skinfold and proceeds posteriorly toward the ischium. This incision allows the retrogluteal flap to be made.

If a posterior modified hemipelvectomy is performed, the wing of the ilium is transected from the sciatic notch to the mid-portion of the ilium. The hypogastric artery is preserved and the external iliac artery is ligated. The decision between a classical hemipelvectomy and a modified posterior flap hemipelvectomy is made preoperatively. In general, modified hemipelvectomies are performed for thigh and groin lesions, whereas classical hemipelvectomies are performed for true pelvic tumors of the muscle or bony structures.

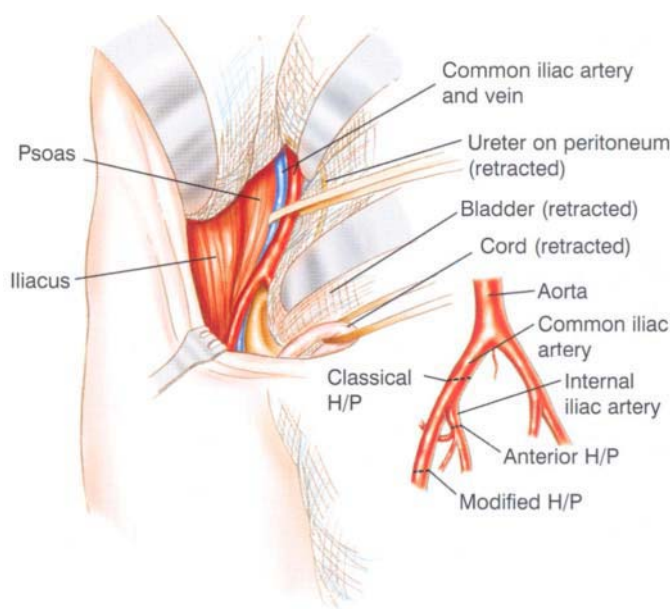


Figure 20.10 Ilioinguinal retroperitoneal incision and approach. The retroperitoneal space is easily entered by detaching the abdominal wall musculature from above the ilioinguinal ligament and off of the iliac crest. For large tumors of the ilium the retroperitoneal space is entered laterally where there is more free retroperitoneal fat. The peritoneum is then reflected off of the tumor mass and the retroperitoneal space is developed. The ureter remains on the peritoneal reflection. The common iliac artery and vein are identified, as well as the internal (hypogastric artery and vein) and the external iliac arteries and veins. It is crucial to identify all of the vascular structures initially to prevent any mistakes in ligation. *Insert:* The levels of transection and ligation of the iliac vessel, along with its two major branches (internal and external iliac vessels) are illustrated. A classical hemipelvectomy requires ligation of the common iliac artery and vein. The modified hemipelvectomy requires preservation of the hypogastric artery and specifically the first branch, the superior gluteal artery. The external iliac artery and vein are ligated. The anterior hemipelvectomy requires the external iliac artery to be intact, which is the main pedicle to the quadriceps muscle. Therefore, the hypogastric artery is ligated at its takeoff from the common iliac artery. The external iliac artery is not ligated.

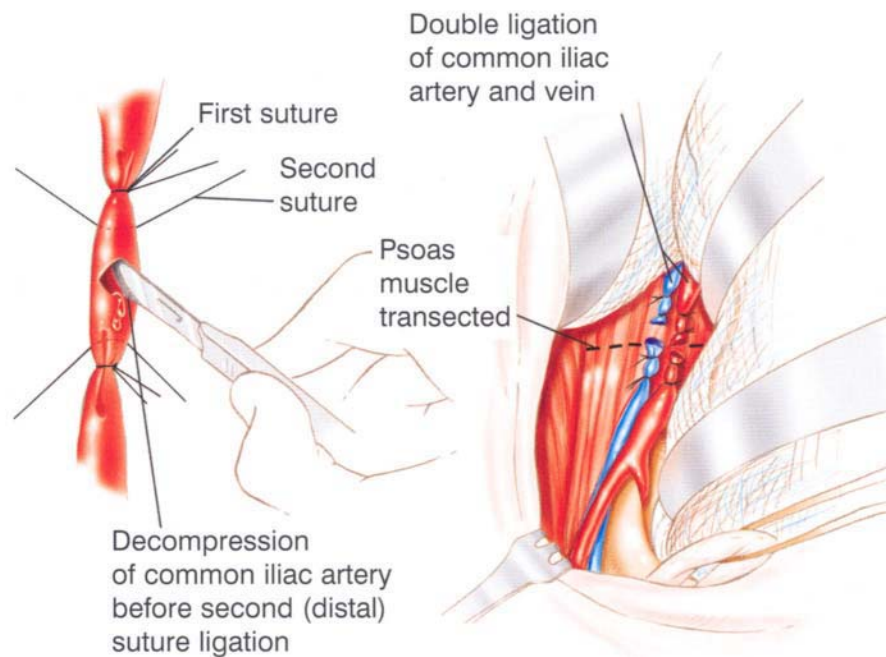


Figure 20.11 Transection of common iliac artery and vein. The peritoneum and its contents are retracted towards the midline with large retractors and the peritoneum is packed off with warm lap sponges. Both the artery and vein are double ligated and transected and oversewn with 3-0 silk sutures. It is extremely important to identify the vascular anatomy correctly before ligating any vessels. In obese patients presenting with large pelvic tumors it may be difficult to identify the vessels. A surgical maneuver that the senior author recommends is to initially transect the psoas muscle proximally through Kelly clamps and then oversew the muscle with chromic sutures. This permits easy exposure of the common iliac vessels and the hypogastric vessels on the medial brim of the pelvis. *Insert:* Technique of major pelvic vessel ligation and transection. Arteries should be doubly ligated and transected. The second set of sutures are not tied until the vessel is decompressed with a knife. Any clots or atherosclerotic plaques should be removed prior to the second suture. This is oversewn with a 3-0 silk ligature. Similarly, large veins are doubly ligated and transected.

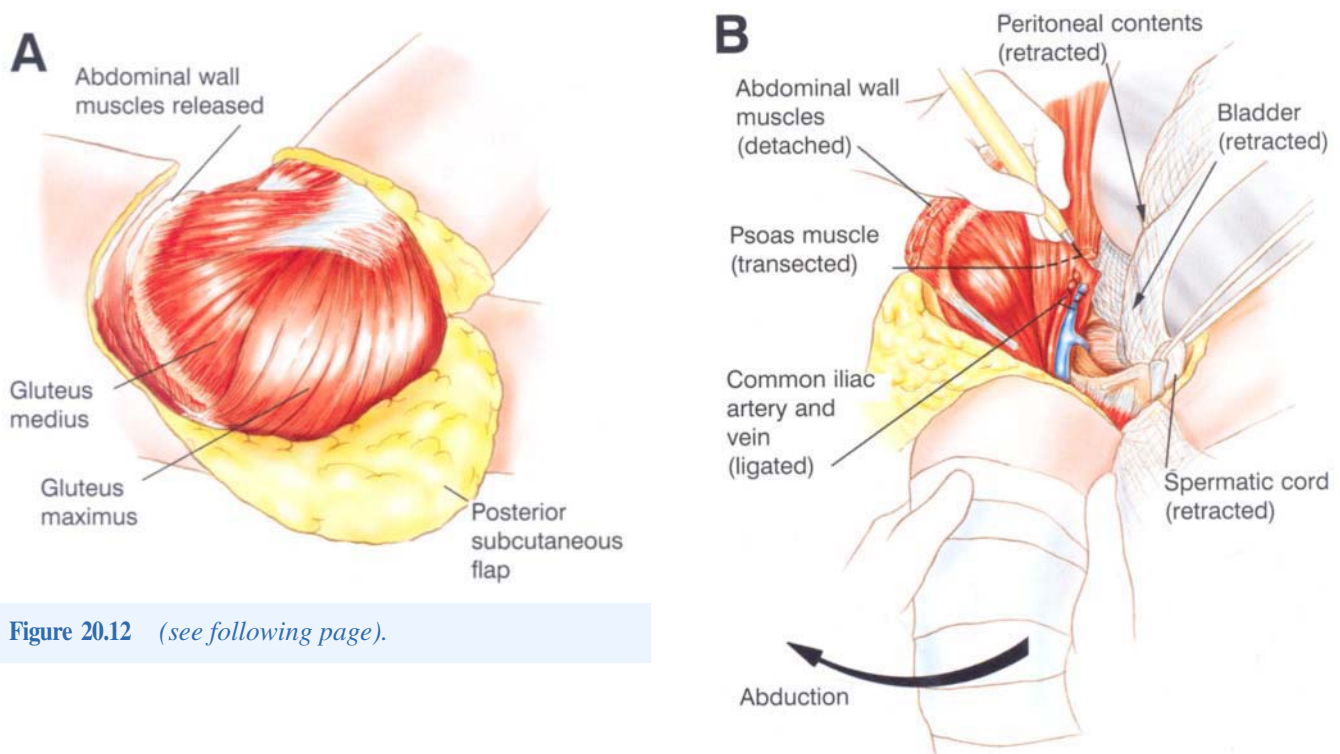


Figure 20.12 (see following page).

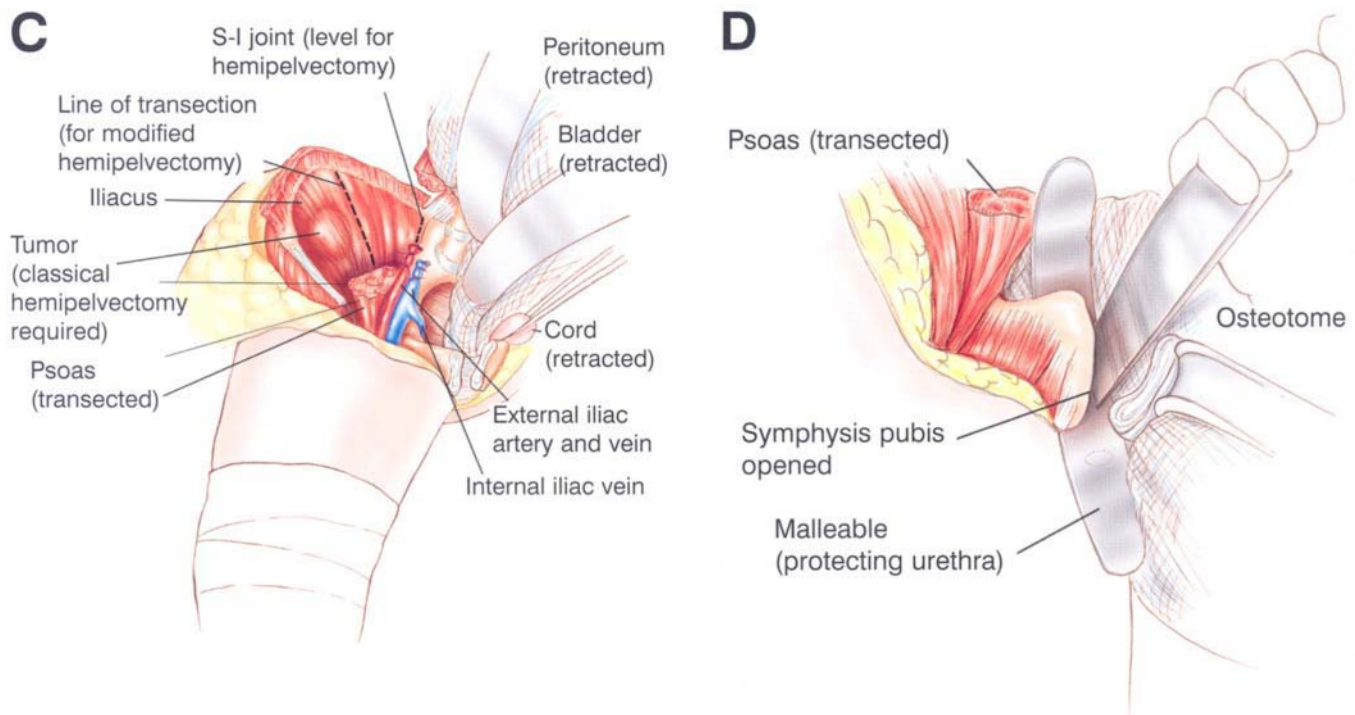


Figure 20.12 Anterior approach and release of psoas and abdominal wall musculature. Through the anterior incision, most of the surgery for a hemipelvectomy should be performed before the perineal and posterior components. (**A**) The abdominal wall musculature is released from the crest of the ilium with a 1–2 cm cuff of muscle remaining along the ilium. (**B**) The psoas muscle has a tendency to bleed postoperatively and should therefore be oversewn. Depending on the type of hemipelvectomy to be performed (classical or modified), the level of the abdominal wall musculature release and the level of the posterior osteotomy will vary. Classical hemipelvectomy consists of a disarticulation of the sacroiliac joint, therefore requiring all of the abdominal musculature to be released up to the paraspinal muscles. The iliolumbar ligament is a good surgical landmark, inserting onto the ilium posteriorly just above the superior aspect of the sacroiliac joint. This is especially useful in obese patients in whom the sacroiliac joint cannot easily be palpated. (**C**) A modified hemipelvectomy is an amputation preserving a portion of the wing of the ilium and the underlying gluteus maximus muscle and its major pedicle the inferior gluteal vessels. Therefore, an osteotomy is performed through the wing of the ilium starting at the sciatic notch. The iliocostus muscle is transected internally and the abductor muscles are transected longitudinally (posteriorly). Note that all of the muscles located anteriorly in the pelvis are transected at this step. The sacroiliac joint is also identified anteriorly and the vessels are mobilized off of the sacroiliac joint in preparation for the sacroiliac disarticulation that is the final step of the operative procedure. (**D**) The perineal incision is then begun prior to abducting or flexing the affected extremity. The symphysis pubis is opened with a small osteotome or a cutting cautery. It is necessary to retract the bladder with a malleable retractor and an additional small malleable retractor is placed beneath the symphysis pubis notch to protect the urethra. The urethra is easily palpable and protected with a Foley catheter in place. For large tumors of the pelvic floor the urethra may be around the pseudocapsule of the tumor. Therefore, great care must be taken not to enter the tumor or the pericapsular structures of the prostate.

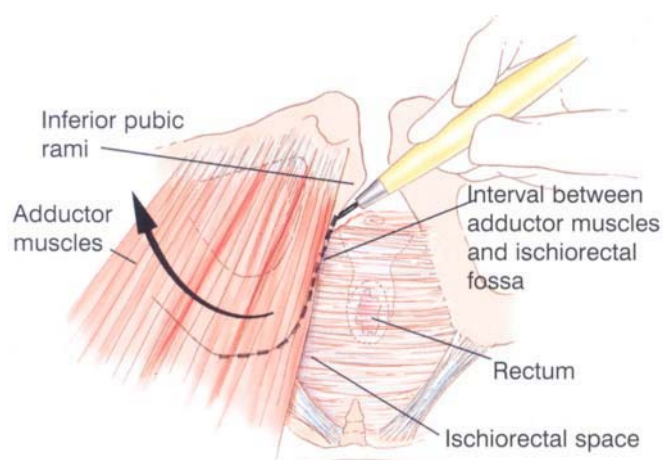


Figure 20.13 (left) Perineal incision. This is the second major step in performing a hemipelvectomy. With the affected extremity flexed and abducted, the surgeon stands between the two legs in order to visualize the pelvic structures. A cutting cautery is utilized to cut along the inferior pubic ramus, taking care not to drift into the adductor muscles. The ischiorectal space is easily entered at this point and is packed off. The incision then extends from the ischium to the symphysis pubis. No attempt to release the pelvic floor musculature is made at this time.

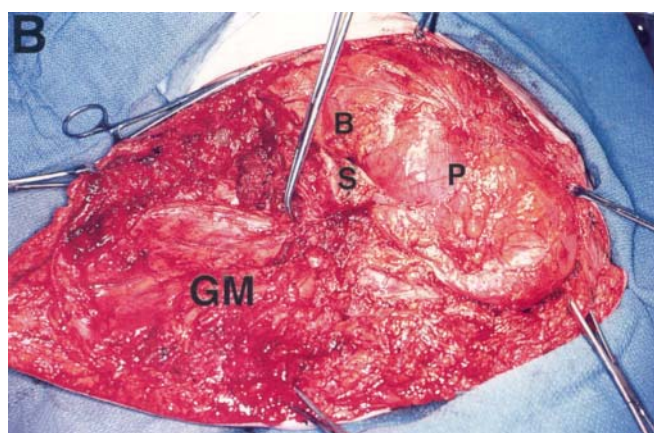
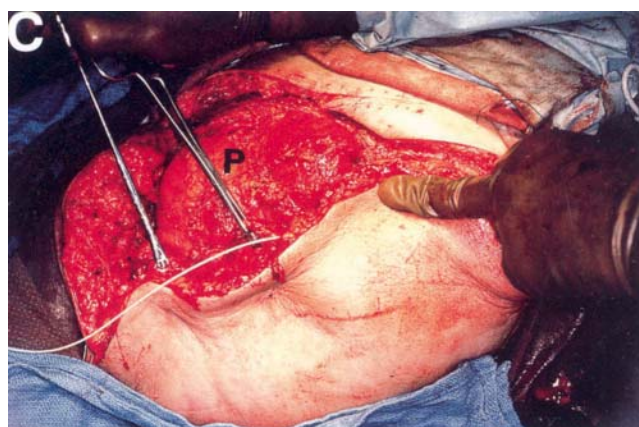
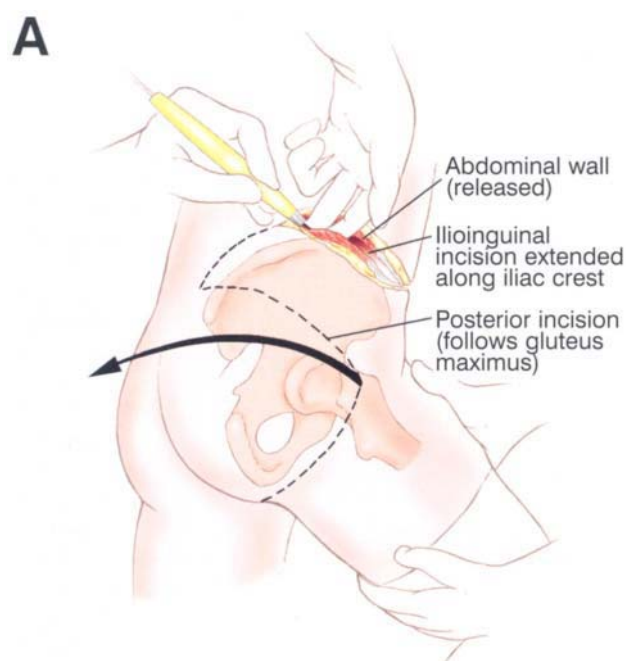


Figure 20.14 Posterior flap development. (A) If the abdominal wall musculature has not been completely released, it is released at this point. The patient is then rotated into a lateral position and the assistant from the other side of the table flexes and adducts the extremity to expose the gluteal area to the surgeon. A posterior flap (classical hemipelvectomy) begins at the superior aspect of the sacroiliac joint and extends along the iliotibial band to the greater trochanter, and then passes posteriorly along the gluteus maximus skinfold. A true classical hemipelvectomy utilizes only a subcutaneous flap. If there is no tumor in the gluteal muscles, then a thick fasciocutaneous flap can be utilized. This is important since it can decrease the amount of postoperative flap necrosis. (B) Intraoperative photograph showing the peritoneum (P), bladder (B), sacrum (S), and a large posterior subcutaneous flap utilized for a classical posterior flap hemipelvectomy. The right angle clamp is on the pedicle to the gluteus maximus muscle (GM). (C) The partial closure of the posterior myocutaneous flap (P) over the retroperitoneal surface.

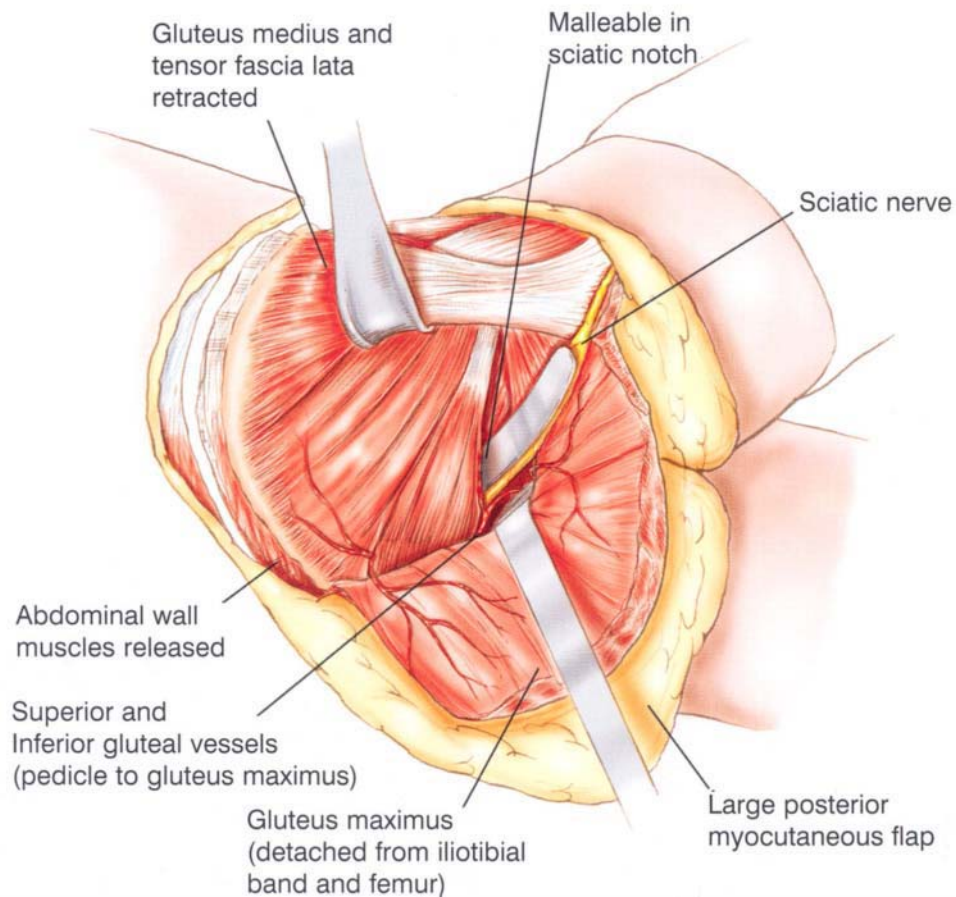


Figure 20.15 Variation of a posterior flap for a modified posterior flap hemipelvectomy. A modified posterior flap hemipelvectomy is an amputation through the wing of the ilium with preservation of the gluteus maximus and its major pedicle, the inferior gluteal vessels. A malleable retractor is placed through the sciatic notch to protect the iliac and the inferior gluteal vessels. The abductors are then transected from the sciatic notch to the mid-portion of the ilium, externally, with a cutting cautery. This is the line of the osteotomy. The iliocapsular muscle, which corresponds to this incision internally, is similarly transected. If it has not already been performed, the iliocapsular muscle is then transected through Kelly clamps. The ilium is then osteotomized with either a high-speed burr or an oscillating saw. If an osteotome is utilized, the surgeon must be extremely careful that the tip of the osteotome does not injure the major vessels or the pedicle to the gluteus maximus.

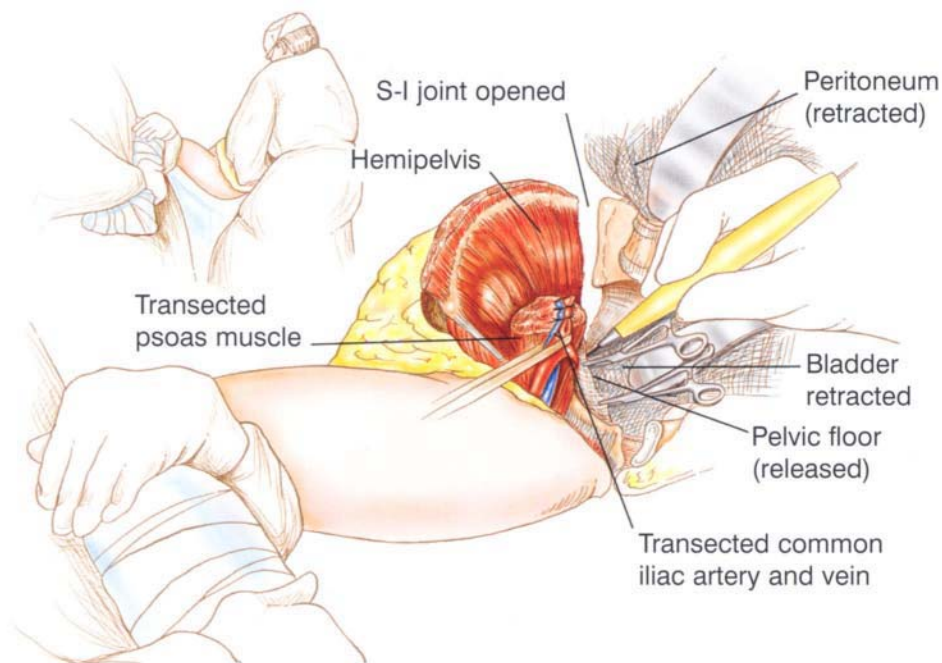
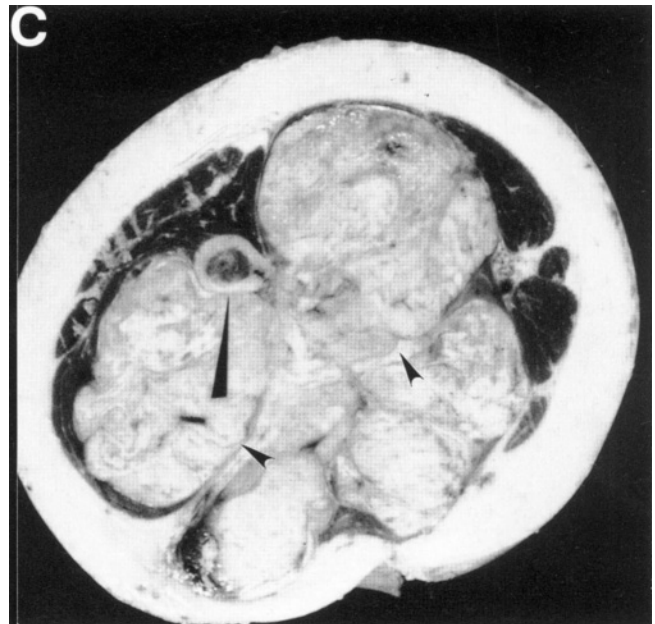
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Figure 20.16 (A) Completion of amputation and release of pelvic floor muscles. The final step of the amputation is the release of the sacroiliac joint and the remaining pelvic sling muscles attaching to the ilium and pelvic floor. The surgical assistant stands on the same side of the table as the surgeon and flexes and abducts the lower extremity to expose the pelvic floor muscles for the surgeon. A sponge on a stick is utilized to push the rectum off of the pelvic sling muscles in the inferior portion of the wound. Note, if a left-sided hemipelvectomy is performed, great care must be taken to mobilize the rectum to avoid injury to it. The sling muscles are clamped with Kelly clamps and transected. The anterior capsule of the sacroiliac joint and occasionally some of the sacrolumbar trunks are the only remaining structures that must be opened and released. Note that the sacroiliac joint is not opened previously due to the potential of bleeding from injury to the perisacral veins. (B) Photograph of a gross specimen following a palliative hemipelvectomy following multiple recurrences for metastatic renal cell carcinoma. A posterior flap hemipelvectomy was performed (small arrows = recurrent tumor, large arrow = intramedullary tract site). (C) Gross specimen following a modified posterior hemipelvectomy for a huge high-grade leiomyosarcoma of the proximal and mid-portion of the thigh. The large arrow denotes the location of the femur. This tumor has crossed several anatomical boundaries (small arrows indicate intervascular septums) to involve the anterior, posterior, and medial compartments of the thigh. Multiple compartmental involvement of the thigh almost always requires the need for a pelvic amputation.

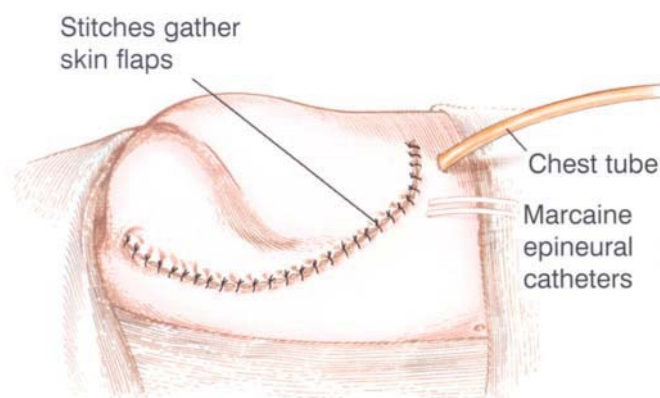


Figure 20.17 Skin closure. A large 28-gauge chest tube is utilized for drainage.

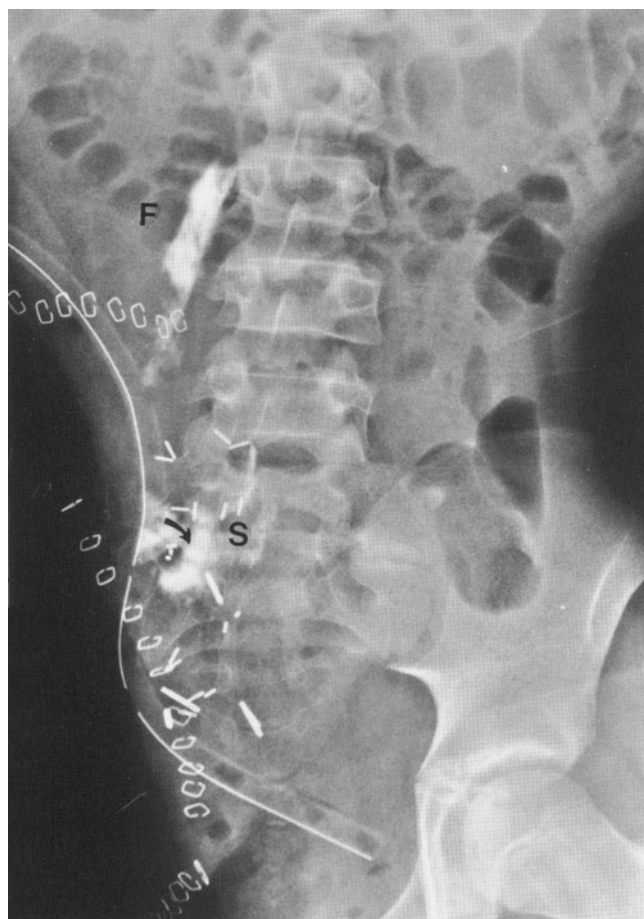


Figure 20.18 Postoperative radiograph of an extended hemipelvectomy (note the sacral alar is absent) with contrast injection of the marcaine catheters that were placed perineurally along the femoral nerve sheath as well as the lumbar sacral plexus. This has been our standard method of postoperative pain control. Perineural marcaine catheters can reduce the need for morphine by approximately 80–90%. They are left in place for 3–5 days. F = femoral nerve; S = sciatic nerve; arrow indicates renografin (contrast) in sciatic sheath.

REHABILITATION AND EMOTIONAL SUPPORT

The cancer patient faces unique psychological problems with hemipelvectomy. Not only is there a threat to the loss of a lower limb and hemipelvis, but also there is a threat to life itself. Rehabilitation of the patient undergoing this major amputation begins at the time of the staging studies. The entire health-care team must develop an honest relationship with the patient and include him or her in the early stages of decision-making. Building upon trust and understanding, the

patient will be better able to accept the amputation and set realistic goals.

All patients undergoing hemipelvectomy will experience considerable phantom limb sensation. This may be a major problem with the hemipelvectomy. As a matter of fact, it may end up being a more disruptive long-term problem to the patient than the loss of the limb itself. The patient should understand that phantom limb sensations are to be expected and that they can be treated with analgesics. It should be emphasized that the discomfort will lessen over time.

The patients who report severe disabling pain are often those who find it most difficult to adapt to surgery and to the malignant process.

Although successful rehabilitation depends to a great extent on the patient's attitude, the physiatrist can help tremendously in these efforts. A *positive attitude* toward functional recovery augmented by early postoperative ambulation (Figure 20.19) may move the patient rapidly to his or her goals. A positive approach is amplified by contact with other patients who have successfully met some of the rehabilitation challenges. This can provide an immeasurable psychological boost to the patient. The oncologist, rehabilitation therapist, and others involved in the postoperative care must coordinate their efforts carefully. There may be conflicting demands on the patient's time. There may be a different interpretation by the patient and family of the same clinical information presented by several different caregivers. The entire team must not only be coordinated but must be positive about the complete rehabilitation that can be achieved following hemipelvectomy.



Figure 20.19 A modern hemipelvectomy prosthesis with a special outer covering to simulate the patient's own skin texture. Note the heavy pelvic band. Weight is transmitted to the ischium as well as around the ribcage. Approximately two-thirds of patients (in the younger age group) having a hemipelvectomy will utilize a hemipelvectomy prosthesis.

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Hip Disarticulation

Paul Sugarbaker and Martin Malawer

OVERVIEW

Hip disarticulation is an amputation through the hip joint capsule, removing the entire lower extremity with closure of the remaining musculature over the exposed acetabulum.

Although performed commonly in the past for malignant bone and soft tissues below the lesser trochanter of the femur, today, the majority of these sarcomas can be treated with limb-sparing procedures. When indicated hip disarticulation provides a low risk amputative alternative that may show function early after the amputation with a modern prosthesis. With intensive physical and rehabilitation patients may become ambulatory with a cane at approximately six months.

INTRODUCTION

Hip disarticulation is the removal of the entire lower extremity through the hip joint. Hip disarticulation has traditionally been performed for osteosarcomas of the distal femur prior to induction chemotherapy in the 1970s. The oncological dogma at that time required that the entire bone be removed due to the existence of intraosseous skip metastases. Therefore, hip disarticulation was the standard operation for distal femoral sarcomas and, similarly, forequarter amputations were the standard operation for proximal humeral sarcomas. Other indications for hip disarticulation today are large diaphyseal tumors that do not extend above the lesser trochanteric area. If the head and neck are involved, a modified hemipelvectomy is required. Otherwise, a high above-knee amputation can be performed. Soft-tissue sarcomas that involve the anterior and posterior thigh in the mid-portion can often undergo a limb-sparing surgical procedure. Approximately 5% of these tumors involve the underlying femur and superficial femoral artery. In such cases an amputation is often required.

Today, in conjunction with the use of adjuvant chemotherapy (induction chemotherapy and/or preoperative radiation therapy for soft-tissue sarcomas), limb-sparing procedures for distal femoral and diaphyseal tumors are extremely successful. Less than 5–10% of patients require an amputation. If an amputation is required for a distal femoral or diaphyseal lesion, a high above-knee amputation can be performed safely. Most soft-tissue sarcomas will respond to induction chemotherapy and/or preoperative radiation therapy with very few requiring an amputation for local control.

This chapter describes the technique developed by the senior author for performing a hip disarticulation in an orderly manner with minimal blood loss. It is applicable to all ages (Figure 21.1).

INDICATIONS/CONTRAINDICATIONS

High-grade sarcomas of the distal femur and diaphysis of the femur can most often be resected with a limb-sparing procedure. Amputation is rarely required. The criteria for limb-sparing resection are given in Chapter 30. This section will summarize the basic contraindications to resection of bony and soft-tissue sarcomas of this anatomic location.

Diaphyseal Bone Tumors with Large Intramedullary Extension

Tumors of the diaphysis may extend extremely long distances proximally and distally. A hip disarticulation

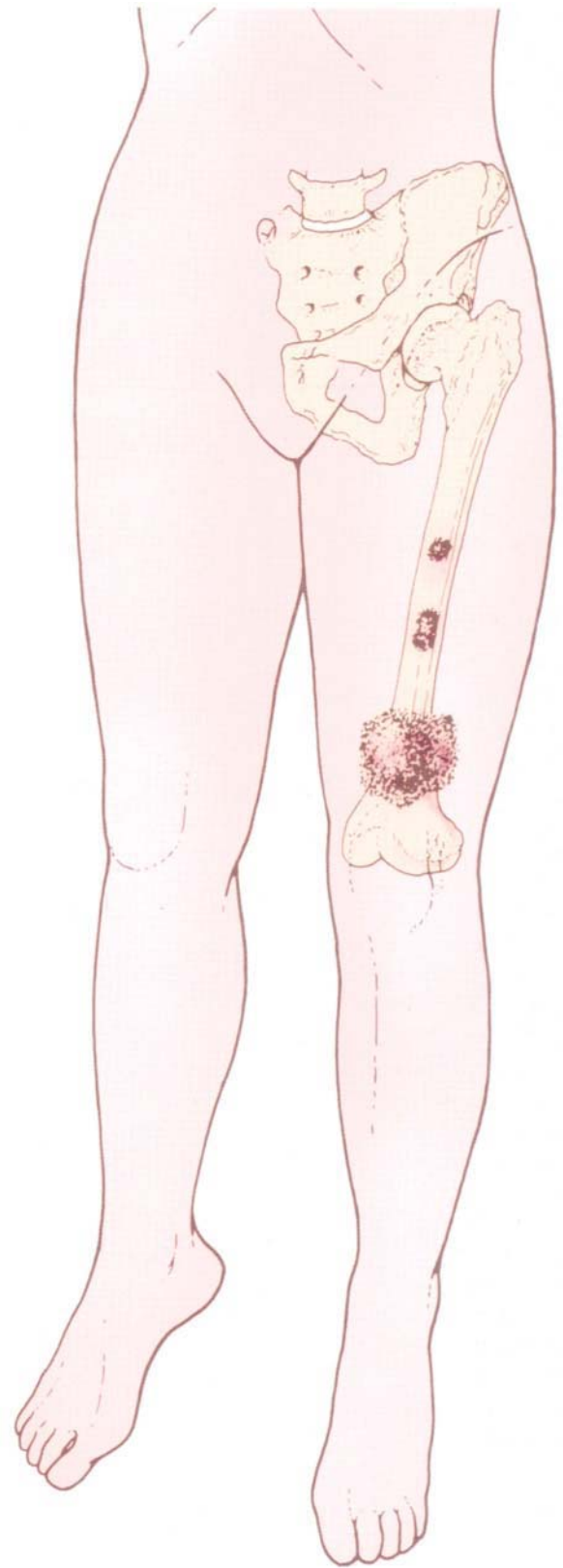


Figure 21.1 Hip disarticulation is indicated for malignant bony and soft-tissue tumors below the lesser trochanter of the femur.

may be required if the intraosseous spread is above the level of the lesser trochanter and the required criteria for limb-sparing surgery are not met. Those tumors that involve the head and neck of the femur require modified hemipelvectomy.

Pathological Fractures of Bone Sarcomas

Fractures that do not respond to induction chemotherapy and cast immobilization with progressive tumor necrosis and fracture healing may require an amputation for local control.

Unresectable Local Recurrences

Local recurrence following limb-sparing procedures and/or radiation therapy around the thigh or distal femur may require hip disarticulation.

Unresectable Soft-tissue Sarcomas

Tumors of the thigh which are extracompartmental involving two or three compartments of the thigh with encasement of the sciatic nerve and/or femoral vessels are deemed Unresectable and are best treated by amputation. If the tumor is below the mid-third of the thigh, a hip disarticulation is adequate. If the tumor is located more proximally, a modified hemipelvectomy is required so as to obtain negative margins.

Extension of the tumor around the hip, ischiorectal space, and sciatic notch must be evaluated in deciding between a hip disarticulation and a hemipelvectomy. Tumors of the proximal thigh most often require a modified hemipelvectomy. Those of the mid-portion of the thigh may be treated by hip disarticulation. It is important to note that there is minimal functional difference between the two procedures. Therefore, the safest procedure is a modified hemipelvectomy. This is an extra-articular amputation on the opposite side of the pelvis with preservation of the gluteus maximus and the ileum. All potentially contaminated structures are removed with this procedure. A hip disarticulation is in general a poor oncological procedure because, despite the imaging studies, tissues that are at risk for local recurrence still persist; that is, the muscle attachments around the hip, the hip joint capsule, and the acetabulum.

STAGING AND IMAGING STUDIES

CT and MRI

CT and MRI are extremely useful in determining tumor extent, especially the proximal extent. The ischiorectal fossa, hip joint, and the groin must be carefully evaluated for additional tumor extension. The MRI is especially useful to evaluate the intraosseous spread of tumor within the marrow. If the tumor is below the level of the lesser trochanter, a high above-knee amputation or hip disarticulation can probably be performed. If the head or neck of the femur is involved by tumor there is a significant risk of joint involvement; therefore a modified hemipelvectomy is required. There have been reports of extra-articular hip resection for tumors of the proximal femur in lieu of modified hemipelvectomy, but this is essentially an extension of a hip disarticulation, that is, an extra-articular resection of the acetabulum en-bloc with the proximal femur.

Bone Scan

Bone scan is useful in determining bony involvement of the femur as well as the involvement of the adjacent pelvis and acetabulum. Acetabular involvement (transarticular metastases) contraindicates a hip disarticulation and is an indication for a modified hemipelvectomy.

SURGICAL GUIDELINES

1. Equal anterior and posterior flaps are utilized. Modification of these flaps may be required depending on the location of the tumor.
2. The femoral triangle is exposed and the common femoral vessels are doubly ligated and transected.
3. The abductors are released from the greater trochanter and the adductors are transected from their origin on the pelvis.
4. The sciatic nerve must be transected high near the sciatic notch.
5. The closure must consist of tenodesing the remaining muscles over the acetabulum.
6. A sciatic epineural catheter is used for postoperative pain relief.

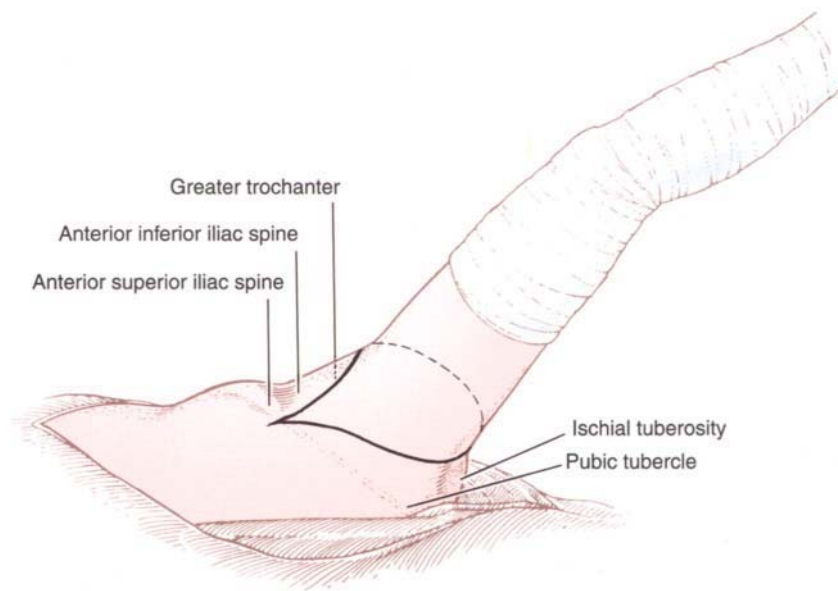


Figure 21.2 Incision. Bony landmarks to be identified include the pubic tubercle, anterior superior iliac spine, anterior inferior iliac spine, ischial tuberosity, and greater trochanter. The anterior portion of the incision commences one fingerbreadth medial to the anterior superior iliac spine. It descends to the pubic tubercle and then over the pubic bone to two fingerbreadths distal to the ischial tuberosity and gluteal crease. If the buttock flap is extremely thick, the anterior portion of the incision should be moved laterally. The posterior portion of the incision extends two fingerbreadths anterior to the greater trochanter and then around the back of the leg distal to the gluteal crease. The distance the incision is beyond the gluteal crease is directly proportional to the anterior-posterior diameter of the patient's pelvis.

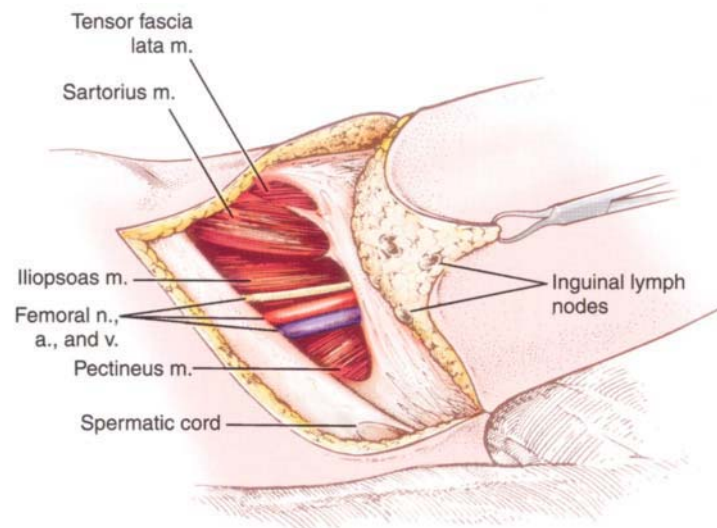


Figure 21.3 Exposure of femoral triangle. The skin is incised, and the dissection is extended through subcutaneous fat and Scarpa's fascia until the external oblique aponeurosis is seen. Multiple venous bleeding points from branches of the saphenous vein are clamped, divided, and ligated. A moderate-sized artery, the superficial epigastric, and multiple branches of the external pudendal vessels must be secured. The superficial inguinal lymph nodes should be moved laterally with the specimen, and the round ligament in the woman, or the spermatic cord in the man, is exposed but not included in the specimen. An Adair clamp is placed securely on the apex of the skin specimen for traction. By making an incision just below the inguinal ligament into the fossa ovalis, the femoral vein, artery, and nerve are widely exposed below the inguinal ligament.

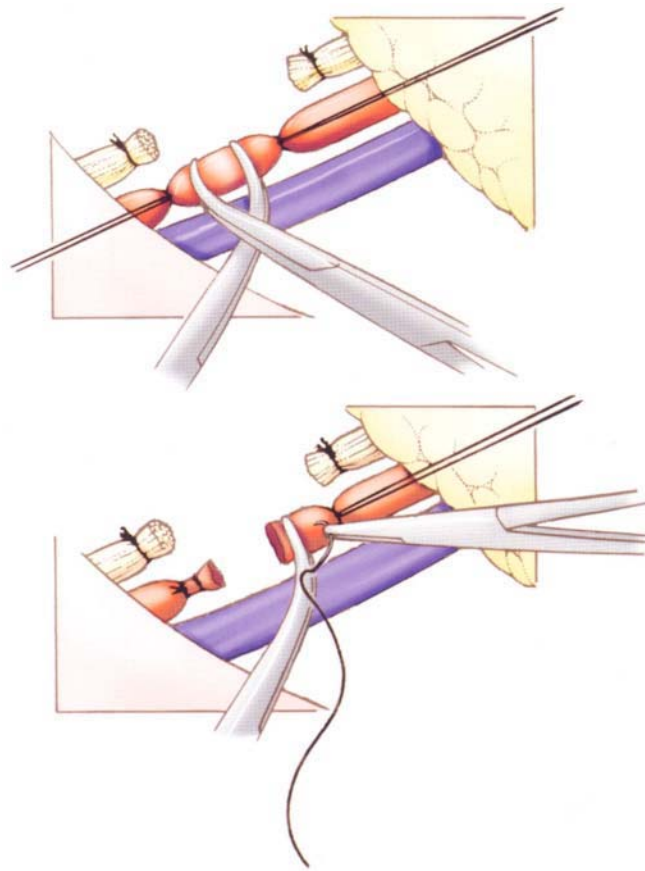


Figure 21.4 Division of femoral vessels and nerve. Individual silk ties are placed around the femoral vessels; first the artery and then the vein are tied in continuity. Right-angle clamps are placed between the ties, and the vessels are severed. The proximal ends of the vessels are further secured by a silk suture ligature placed proximal to the right-angle clamps. The femoral nerve is placed on gentle traction and ligated at its point of exit from beneath the inguinal ligament. When the femoral nerve is severed, it retracts beneath the external oblique aponeurosis, so that if a neuroma forms it will not be in a weight-bearing portion of the stump.

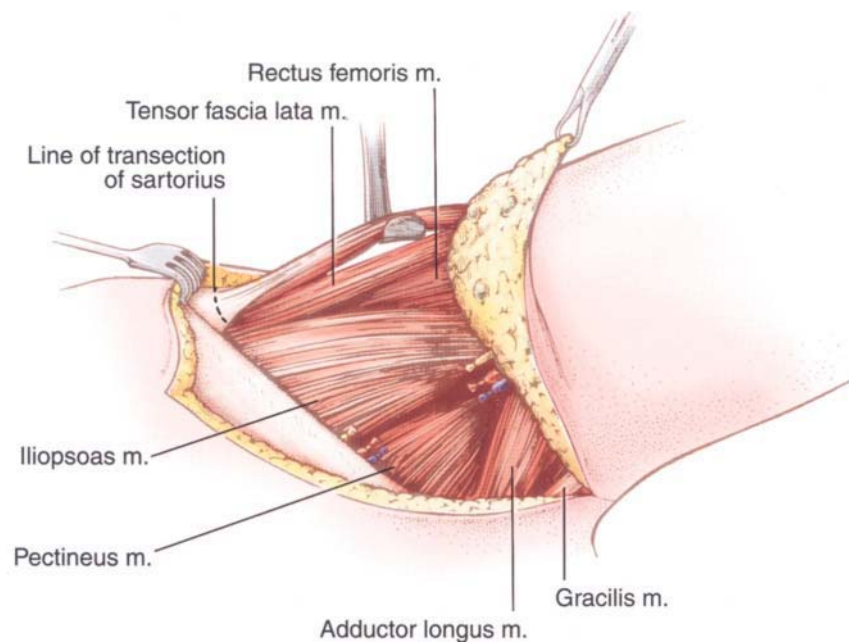


Figure 21.5 Division of sartorius muscle and femoral sheath. The sartorius muscle is located as it arises from the anterior superior iliac spine. It is dissected free from the surrounding fascia and then transected from its origin on the spine by electrocautery. The femoral sheath and fibroareolar tissue posterior to the femoral vessels are also incised by electrocautery. This dissection exposes the hip joint capsule.

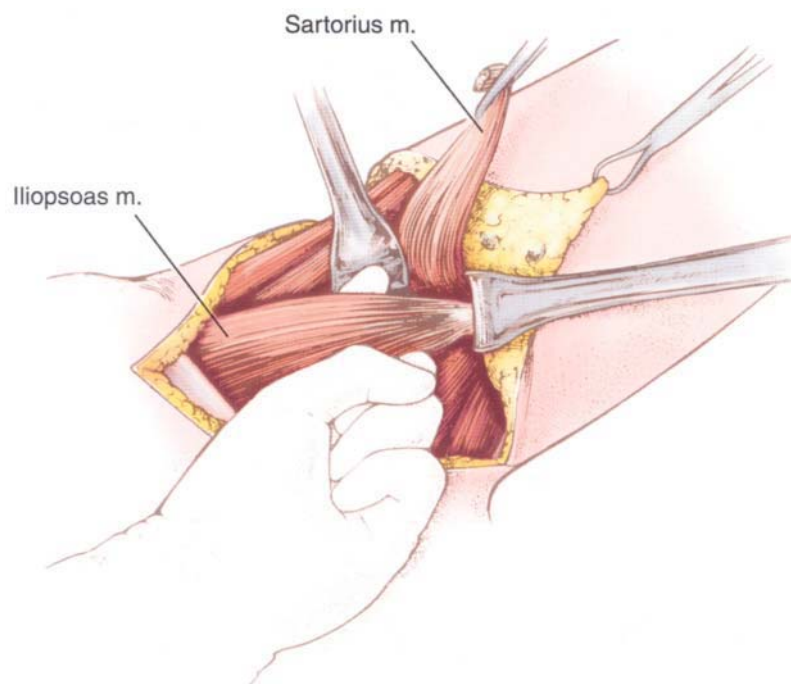


Figure 21.6 Division of iliopsoas muscle at its insertion. The hip is flexed slightly to relax the iliopsoas muscle. It is then possible to pass a finger around the iliopsoas muscle in a mediolateral blunt dissection. If an attempt is made to pass the finger beneath the muscle from lateral to medial, the very intimate attachments between the iliopsoas muscle and the rectus femoris muscle prevent this from being easily done. By sharp and blunt dissection the entire iliopsoas muscle is dissected until its insertion on the lesser trochanter is clearly defined. Several vessels of prominent size pass from the anterior surface of this muscle, and care should be taken to secure these vessels prior to their division. The iliopsoas muscle is severed at the level of its insertion onto the lesser trochanter.

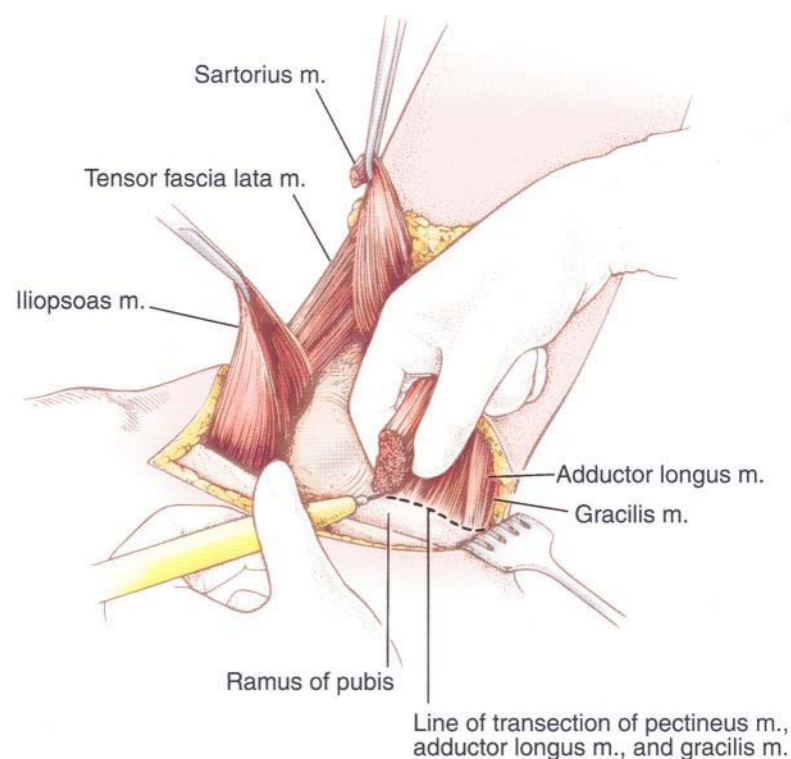


Figure 21.7 Transection of pectineus muscle at its origin. Now attention is turned to the adductor muscles and their release from the pelvis. It is important to note that this dissection proceeds from lateral to medial around the extremity. To preserve the obturator externus muscle on the pelvis, locate its prominent tendon arising from the lesser trochanter. Locating this tendon identifies the plane between pectineus muscle and obturator externus; a difference in the direction of the muscle fibers of these two muscles is also apparent. A finger is passed beneath the pectineus muscle, and it is released at the level of its origin from the pubis by electrocautery. Beneath the pectineus muscle numerous branches of the obturator artery, vein, and nerve can now be visualized.

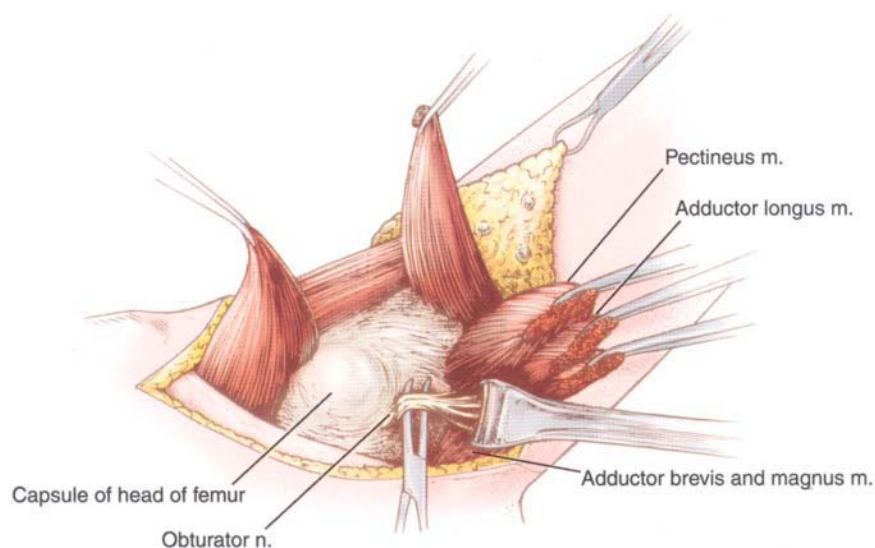


Figure 21.8 Transection of gracilis, adductor longus, brevis, and magnus muscles from their origin; division of obturator vessels and nerve. The remainder of the abductor muscles are transected at their origin on the symphysis pubis. These include the gracilis, adductor longus, adductor brevis, and adductor magnus muscles. Note that the obturator vessels and nerves usually bifurcate around the adductor brevis muscle. It is important that branches of the obturator artery be identified and secured during the dissection, to prevent accidental rupture and retraction of the proximal ends up into the pelvis.

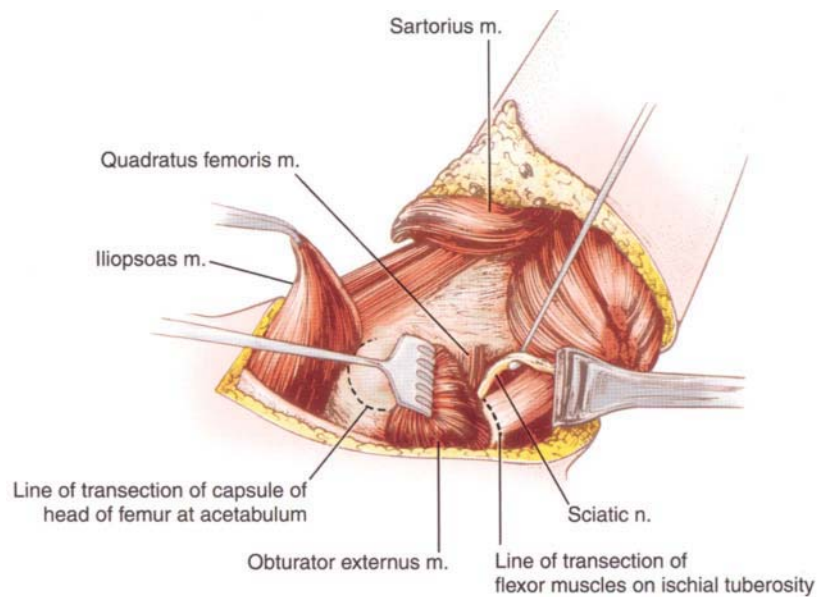


Figure 21.9 Release of muscles from the ischial tuberosity. The extremity is hyperabducted to help localize the ischial tuberosity and to retract the cut ends of the abductor muscles. The flexor muscles, sciatic nerve, and quadratus femoris muscle are now identified. The large circumflex femoral vessels are nearby and should be avoided. The semimembranosus, semitendinosus, and long head of the biceps muscle are transected from their origin on the ischial tuberosity while preserving the quadratus femoris muscle and sciatic nerve.

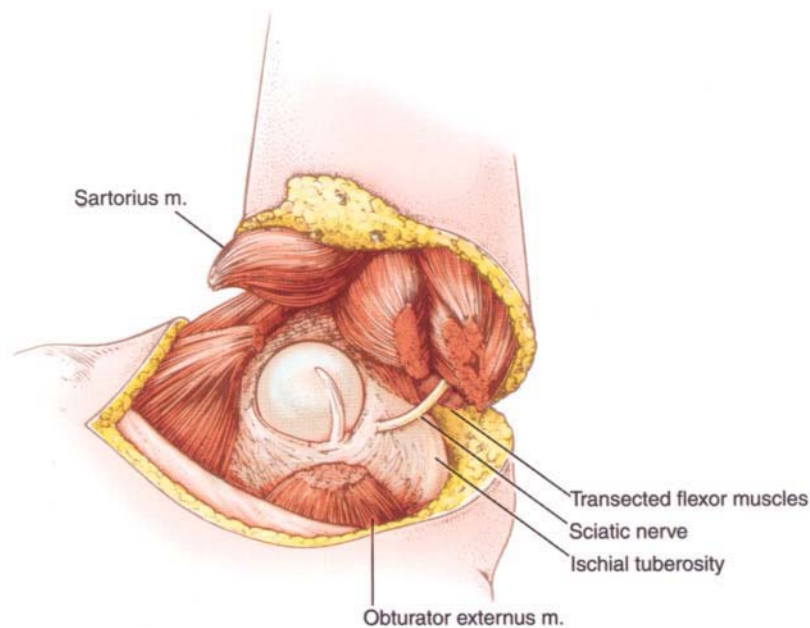


Figure 21.10 Incision of the anterior portion of the hip joint capsule. At this point all the anterior and posterior muscle groups have been divided. The joint capsule overlying the head of the femur is incised, and the ligamentum teres is transected by electrocautery.

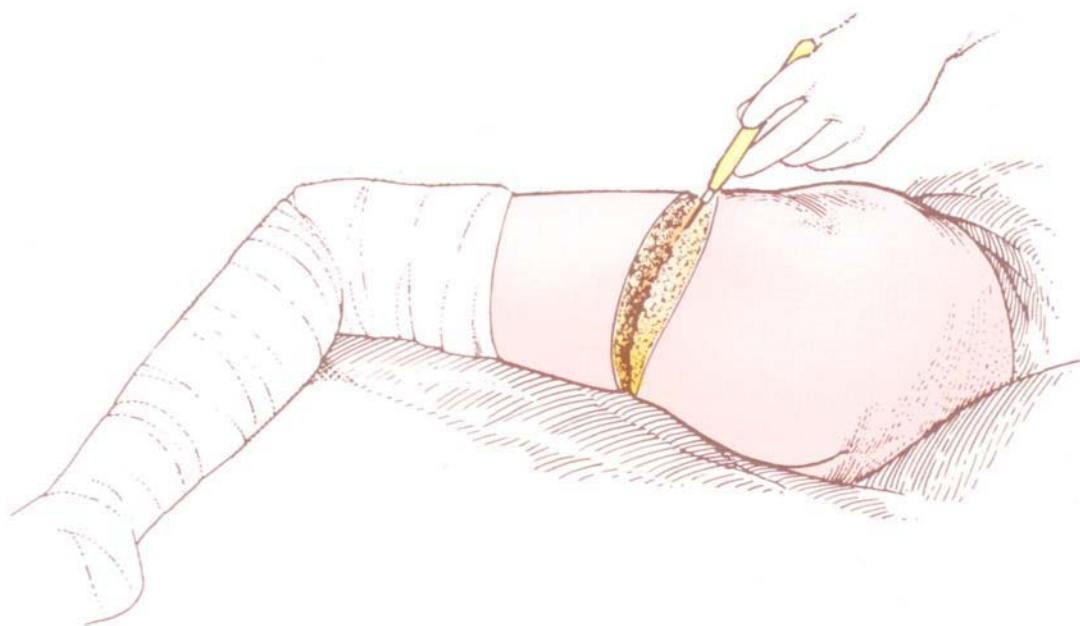


Figure 21.11 Completion of the skin incision. The surgeon now moves from a position anterior to the patient to a posterior position. The patient's torso is tilted from posterolateral to anterolateral, and the skin incision is completed down through gluteal fascia.

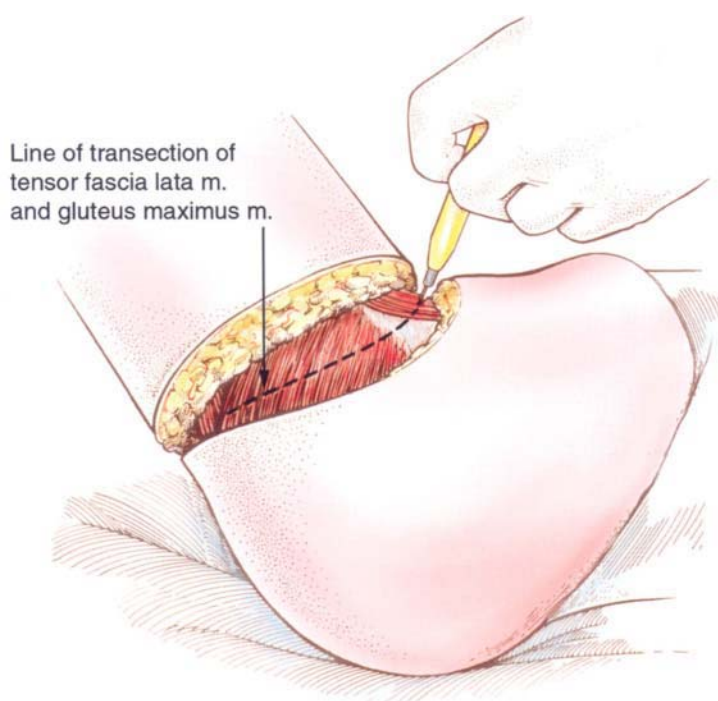


Figure 21.12 Division of tensor fascia lata, gluteus maximus, and rectus femoris muscles. The tensor fascia lata and gluteus maximus muscles are divided in the depths of the skin incision. These are the only muscles not divided at either their origin or insertion in the procedure. Directly beneath these muscles is the rectus femoris muscle, which is transected at its origin on the anterior inferior iliac spine by electrocautery.

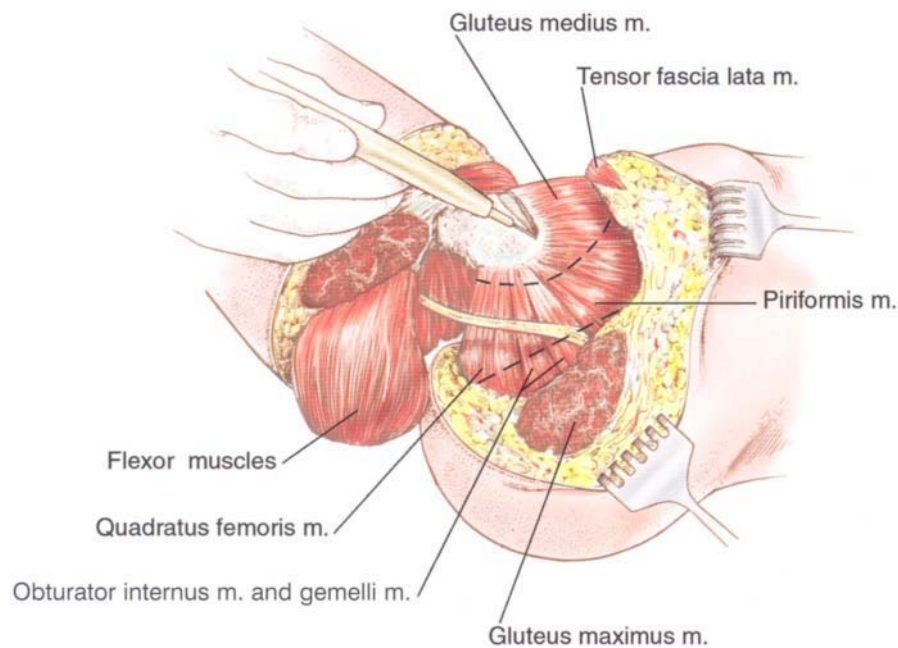


Figure 21.13 Transection of the muscles inserting into the greater trochanter. After division of the gluteus maximus muscle the common tendon containing the multiple muscles inserting into the greater trochanter is exposed. This tendon receives contributions from the gluteus medius, gluteus minimus, piriformis, superior gemellus, obturator internus, inferior gemellus, and quadratus femoris muscles. These muscles are divided close to their insertions on the greater trochanter by electrocautery.

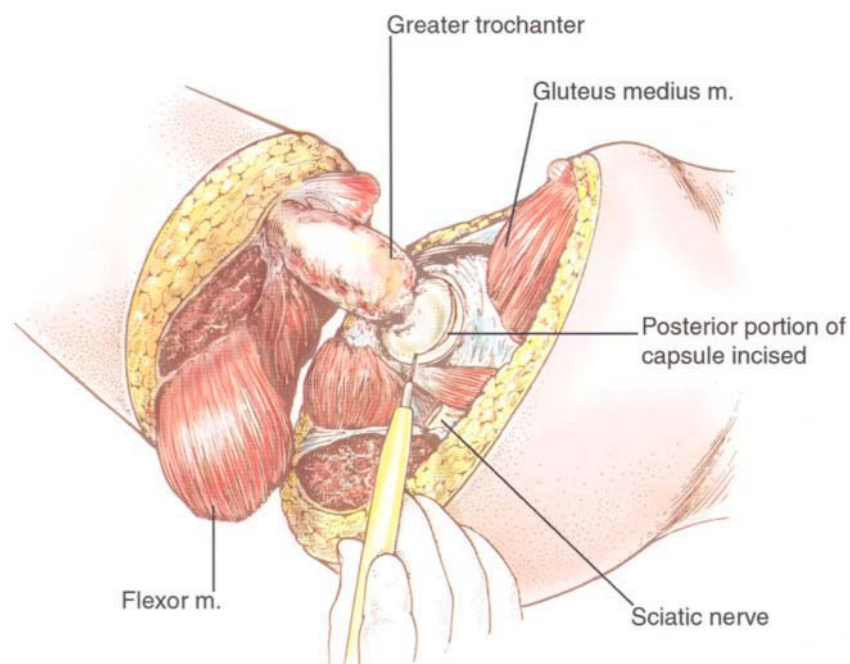


Figure 21.14 Release of specimen. Transection of the hip joint capsule is completed by incising the posterior portion of the capsule. The sciatic nerve is dissected free of surrounding muscle, transected, and allowed to retract beneath the piriformis muscle.

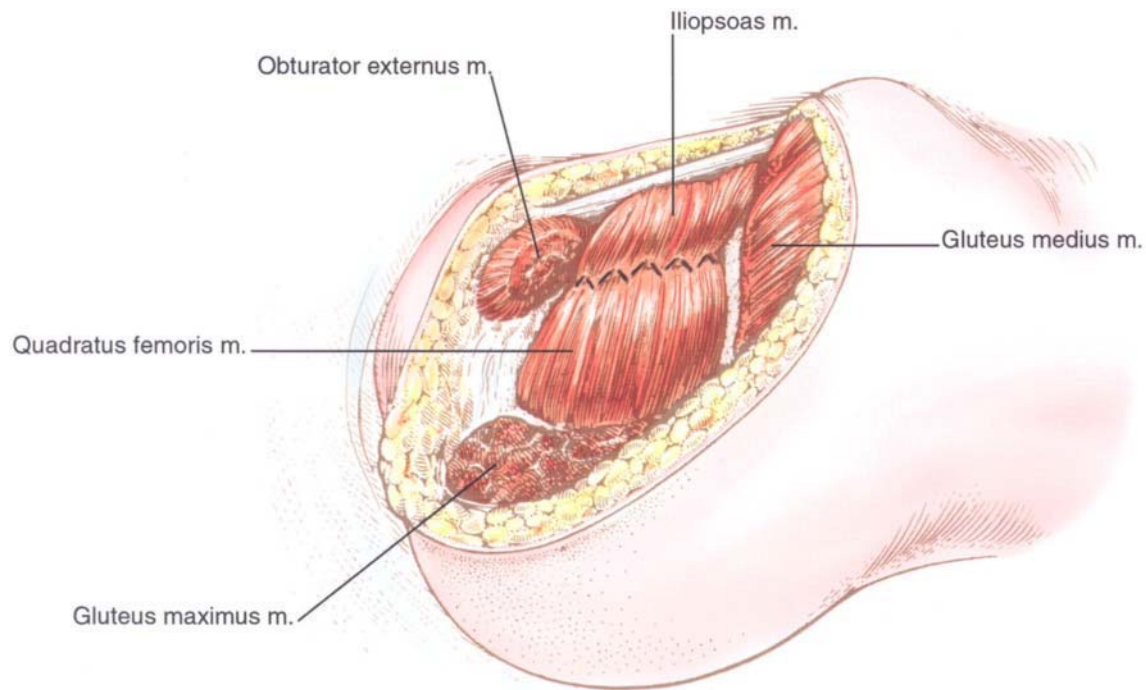


Figure 21.15 Approximation of obturator externus and gluteus medius over the joint capsule. To help provide soft-tissue coverage of bony prominences, the obturator externus and gluteus medius muscles are sutured together over the acetabulum.

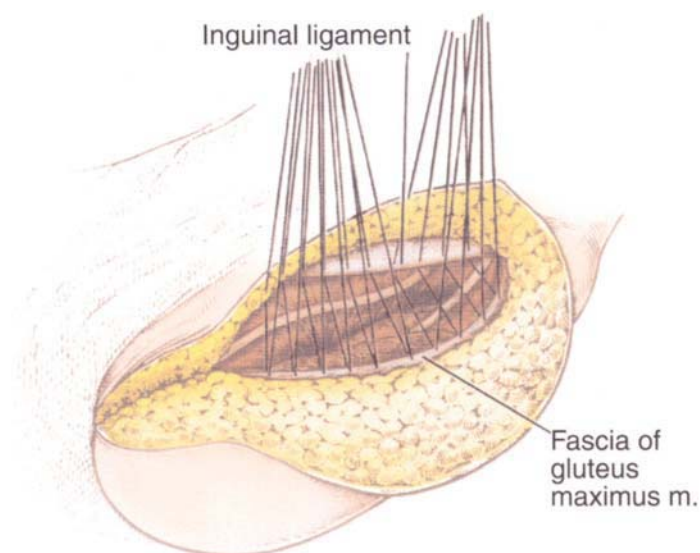


Figure 21.16 Approximation of gluteal fascia to the inguinal ligament and pubic ramus. The gluteal fascia is elevated and secured to the inguinal ligament and pubic ramus. In doing this it becomes apparent that the posterior myocutaneous flap is much longer than the anterior fascia; therefore, multiple stitches are placed that bisect the fascial edge and uniformly gather the gluteal fascia as it is secured to the inguinal ligament.

Sutures are individually placed and then tied. Prior to closure suction catheters are placed beneath the gluteal fascia.

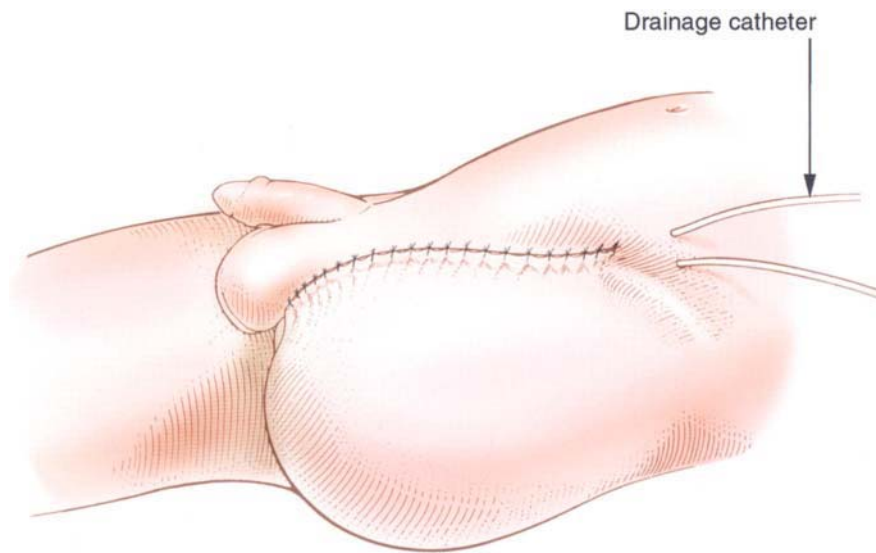


Figure 21.17 Skin closure. The skin is closed with interrupted sutures. Again, care is taken to make sure that there is equal distribution of the excess tissue of the posterior flap. Not infrequently, additional suction catheters must be used to obliterate space within the subcutaneous tissue when the buttock flap is thick. Patency of the suction catheters must be maintained until drainage is diminished. Ambulation may proceed if the patient's hemodynamic status permits on the first postoperative day.

DISCUSSION

Hip disarticulation is an amputation through the hip joint capsule, removing the entire lower extremity, with closure of the remaining musculature over the exposed acetabulum. Hip joint disarticulation was the classic procedure for the treatment of distal femoral osteosarcomas. The oncological thinking during the 1970s was that the existence of skip metastases throughout the intraosseous extent of the femur was extremely significant and a cause of local recurrence and metastatic disease. Therefore, the philosophy of the day (1960s–1970s) was to remove the entire bone when involved by an osteosarcoma. Tumors of the distal and proximal femur were treated by total femur resection/removal; that is, a hip disarticulation. Similarly, an osteosarcoma of the proximal humerus was treated with a forequarter amputation to remove the entire humerus.

Fortunately, today, hip disarticulations are rarely performed for tumors of the distal femur. Ninety to 95% of distal femoral sarcomas can be treated with limb-sparing procedures. Those that cannot are treated with a mid-thigh to a high above-knee amputation. Soft-tissue sarcomas, which involve the distal or mid-portion of the thigh, can often be treated by a limb-sparing resection. A hip disarticulation for a soft-tissue sarcoma is rarely performed; although, similar to bone sarcomas, it was the standard operation for mid-thigh, high-grade soft-tissue sarcomas during the 1960s and 1970s.

It must be noted that tumors that involved the proximal femur are best treated by a modified hemipelvectomy. A hip disarticulation would leave extremely close or positive margins along the remaining hip capsule and/or the musculature around the hip joint that attaches to the ilium anteriorly and posteriorly.

Today, most diaphyseal femoral tumors are treated with an intercalary resection or total femoral replacement. An intercalary resection can be reconstructed with a composite, consisting of an allograft spanned with an intramedullary rod, or an allograft spanned by an autogenous fibula from the same side. MRI is extremely useful in determining the intraosseous extent of diaphyseal tumors.

Today hip disarticulation is considered a poor oncological operative procedure. Its main use is for failed vascular procedures following multiple lower-level amputations, or for massive trauma with crush injuries to the lower extremity.

The surgical technique is based upon a wide fish-mouth incision placed over the central aspect of the femoral triangle. This incision passes medial and lateral at the level of the greater trochanter and then transverses around the posterior thigh. The femoral vessels are initially exposed, ligated, and doubly transected. The medial and lateral thigh musculature is transected above the level of the greater trochanter. The adductor attachments of the muscles are removed from their origin along the ischium and pubic rami.

The hip is then flexed and the posterior incision is made. The posterior musculature is released from the ischium. The sciatic nerve is cut high above the profundus to allow it to retract. The inferior and superior gluteal vessels are ligated prior to removal of the extremity. We routinely utilize epineural marcaine catheters placed into the sciatic and femoral nerves at the time of surgery for postoperative pain control. It has been our experience that this dramatically reduces the amount of postoperative narcotics by 90%. This is especially true in younger patients who have extreme pain following amputations at any level. This catheter is continued for a minimum of 3–5 days postoperatively and, if necessary, the patient can go home with the catheter in place with a portable infusion pump (these pumps are made by several manufacturers).

Function following a hip disarticulation with a modern prosthesis is acceptable. Patients are ambulatory at approximately 6 months with the use of one cane. Intensive physical therapy and psychological rehabilitation is required prior to and following surgery, for optimal results. We routinely transfer patients to a rehabilitation hospital immediately after surgery for a 2-week period of intensive therapy. Patients are instructed in the use of crutches and a walker, and are taught how to wrap their stump. This, in conjunction with a support group for amputees and sarcoma patients, has been found to be beneficial. Early and intensive psychological and physical rehabilitation results in most patients being completely independent and ambulatory at the end of 1 year. Surprisingly, all patients who require amputation at the hip-joint level for vascular disease can also become functional with crutches and/or a wheelchair. Amputations performed for vascular disease are often on a semi-emergency basis. The typical patient is in sepsis from multiple failed above-knee procedures or clotted femoral–popliteal grafts.

Above-knee Amputation

Paul Sugarbaker, Jacob Bickels and Martin Malawer

OVERVIEW

Above-knee amputation is most often performed for advanced soft-tissue sarcomas of the distal thigh and leg, or for primary bone sarcomas of the distal femur and proximal tibia. It is usually indicated because of major involvement of the main neurovascular bundle or the presence of an extensive involvement of the soft tissues. Above-knee amputations may be performed through the distal aspect of the femur (supracondylar), the middle section of the femur (diaphyseal), or just below the lesser trochanter (high above-knee).

The clinical and surgical considerations surrounding above-knee amputations, as well as details of the surgical technique, are described in this chapter. Emphasis is on flap design and meticulous dissection, use of continuous epineural analgesia, myodesis of the major muscle groups to the distal femur, meticulous wound closure, and application of a rigid dressing.

INTRODUCTION

Until recent decades, lower-extremity amputation was the standard method of treatment for most soft-tissue and bone sarcomas. Since then, better understanding of the biological behavior of these tumors and advances in surgical technique, bioengineering, radiographic imaging, radiotherapy, and chemotherapy have led to the advent of limb-sparing surgery.¹ Preoperative chemotherapy, given via the intravenous or intra-arterial route or using isolated limb perfusion, has been found to reduce tumor size, cause significant tumor necrosis, and make previously unresectable tumors amenable to limb-sparing procedures.^{2,3} Limb-sparing surgery is now the standard of care for bone and soft-tissue sarcomas of the extremities and is performed in approximately 90% of all cases (Figure 22.1). All patients must be considered and evaluated for limb-sparing surgery, and the decision to proceed with an amputation should be made on a case-by-case basis. Such decisions are based on local anatomic considerations, tumor grade and stage, and consideration of the functional and psychological impact of the procedure.

GENERAL INDICATIONS FOR LOWER EXTREMITY AMPUTATION

Considerations and indications to be borne in mind when deciding whether amputation is advisable are as follows:

1. *Local recurrence* was once considered a primary indication for amputation; however, local recurrence of a soft-tissue sarcoma has now been shown to have a minimal impact on patient survival.⁴ The capability to resect the recurrent tumor without compromising the function of the extremity should, therefore, be the determining factor on which the decision to amputate is based. Although the applicability of these findings to primary bone sarcomas is questionable, most orthopedic oncology centers treat local recurrence of a primary bone sarcoma in the same manner, and the mere presence of a recurrent tumor is not an indication for an amputation (Figure 22.2).
2. *Major vascular involvement.* Invasion of a major blood vessel by a sarcoma is generally indicative of a poor prognosis. In the past the increased morbidity of a limb-sparing surgery with a vascular graft made amputation the procedure of choice in most of these cases. Because of the availability of reliable vascular grafts, vascular involvement *per se* is no longer an indication for an amputation.⁵ It is the concomitant involvement of a major nerve and the expectation that function of the extremity will be poor that rule out the possibility of limb-sparing surgery.
3. *Major nerve involvement* often occurs within the popliteal space. In general, one nerve may be removed, but a two-nerve deficit results in a poorly functioning extremity. Most patients with such a deficit who have undergone a limb-sparing procedure report that a useless extremity is worse than no limb at all. Nerve involvement is usually combined with a major vascular involvement, and the combination of the two makes amputation the recommended treatment.
Amputations are rarely performed for extensive, neglected benign lesions. In these cases it is the extensive bone destruction, lack of soft tissues for reconstruction, and neurologic compromise that indicate the need for amputation (Figure 22.3).
4. *Soft-tissue contamination* as a result of pathologic fracture through a bone sarcoma or of a poorly performed biopsy was also once considered an indication for amputation. The efficacy of the current chemotherapy regimens makes the limb-sparing procedure a safer option in minor cases of contamination; however, the extent of soft-tissue resection and flap design often have to be modified.⁶ Magnetic resonance imaging (MRI) allows one to evaluate the full extent of a hematoma and plan a limb-sparing procedure. Amputation is usually inevitable in extensive hematomas.
5. A *poorly planned biopsy* can interfere with limb-sparing surgery. The biopsy incision and tract are assumed to harbor tumor cells, and therefore have to be excised en-bloc with the primary tumor and with the same wide margins. The diameter of the biopsy tract and the associated hematoma determine the extent of soft-tissue resection. Amputation is indicated if, following excision of the biopsy tract, the viability of the muscle flaps or function of the extremity would be significantly impaired. Core needle biopsies are strongly recommended in the evaluation of soft-tissue and bone lesions. The hazards of the recommendations for execution of a musculoskeletal tumor biopsy are discussed in Chapter 2.
6. *Infection*, either superficial or deep, is usually the result of tumor ulceration through the skin or infection at the biopsy site. It may negate the possibility of limb-sparing surgery, especially if prosthetic materials will be used. In addition, an infection will impair the ability to administer adequate preoperative and postoperative chemotherapy. Limb-sparing surgery is feasible only if the infection is completely controlled prior to surgery, or if the infected tissues can be completely removed at surgery.
7. *Skeletal immaturity* is still considered a major problem because significant leg-length discrepancy may occur following limb-sparing surgery that involves a

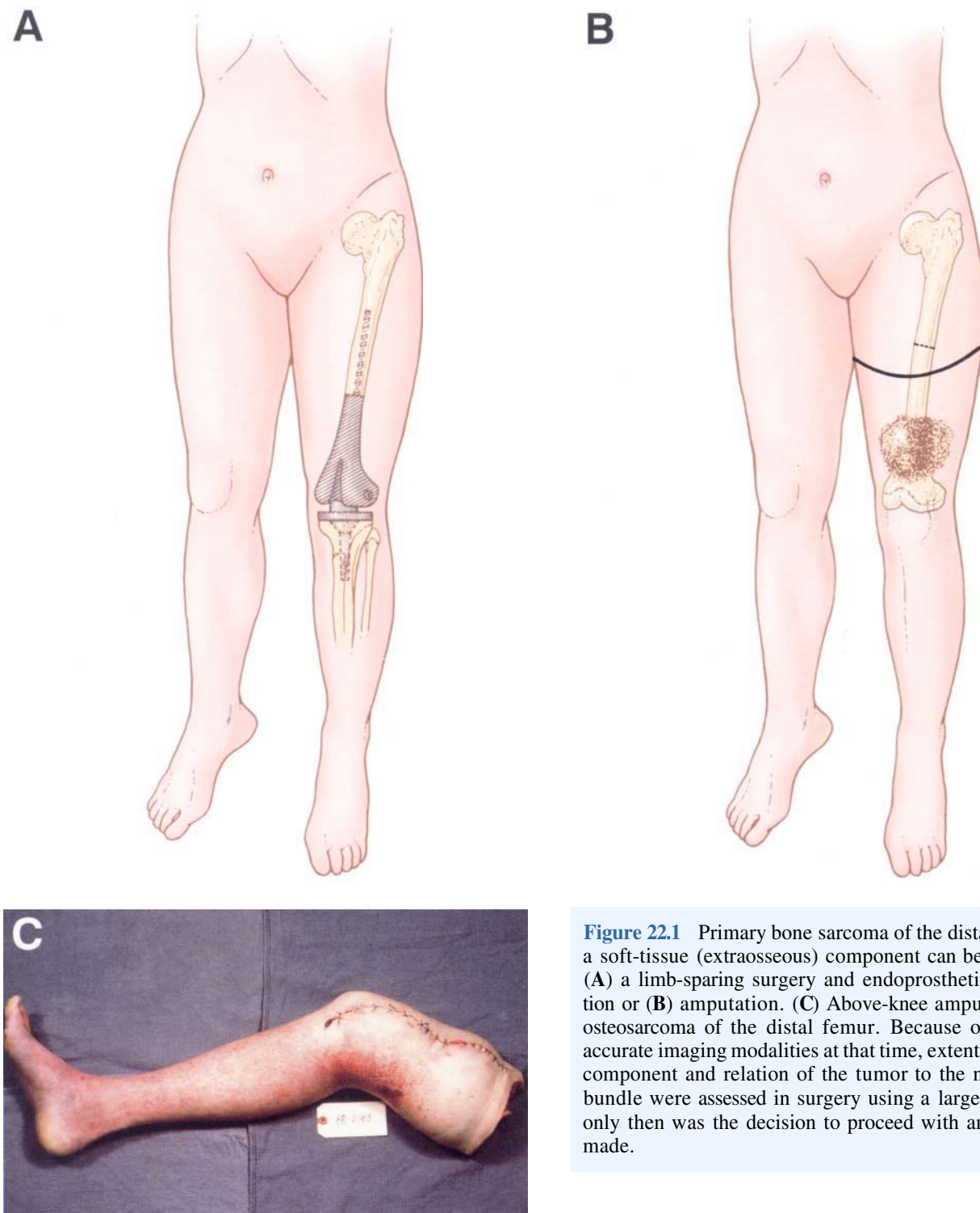


Figure 22.1 Primary bone sarcoma of the distal femur with a soft-tissue (extraosseous) component can be treated with (A) a limb-sparing surgery and endoprosthetic reconstruction or (B) amputation. (C) Above-knee amputation for an osteosarcoma of the distal femur. Because of the lack of accurate imaging modalities at that time, extent of soft-tissue component and relation of the tumor to the neurovascular bundle were assessed in surgery using a large incision, and only then was the decision to proceed with an amputation made.

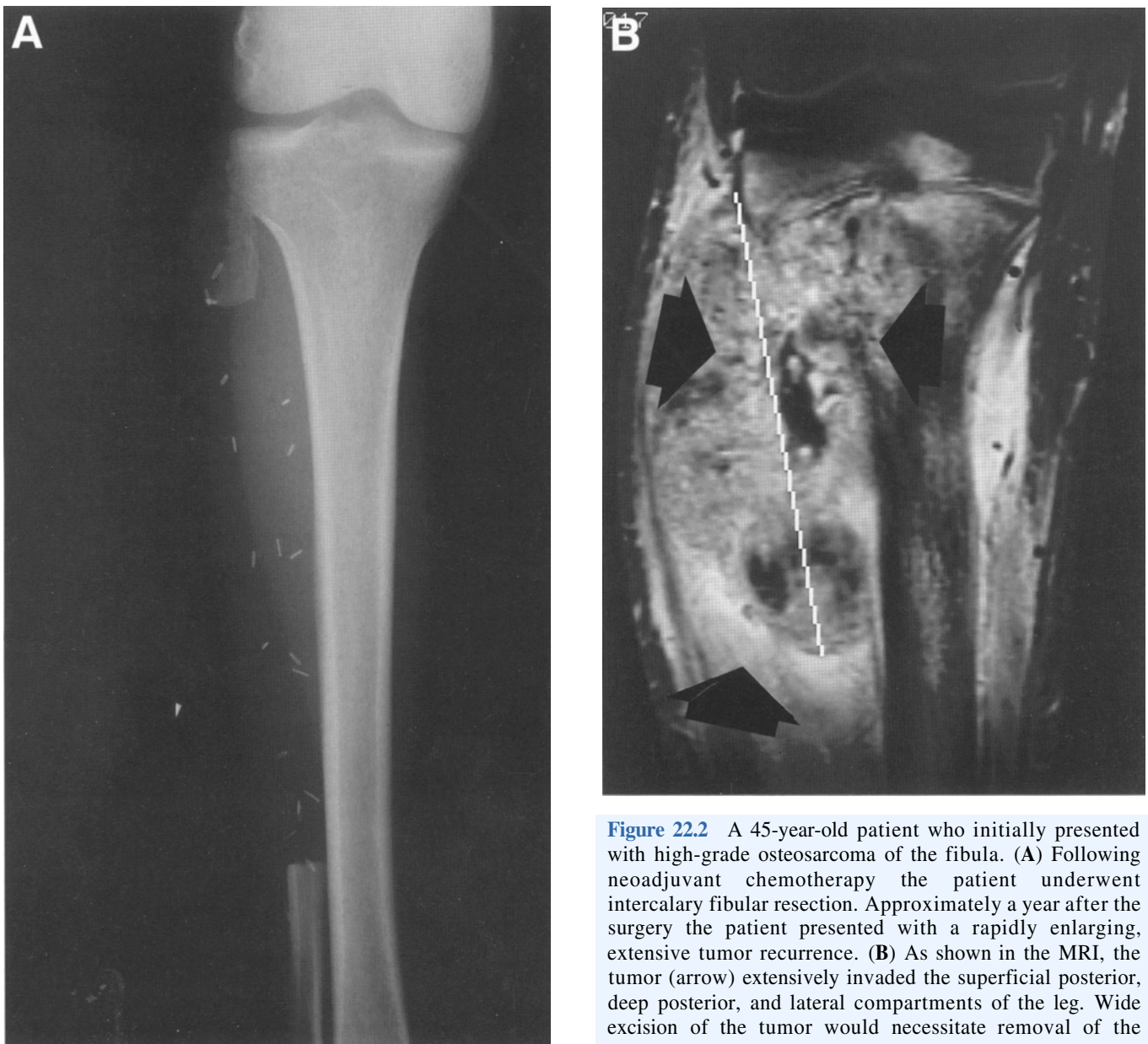


Figure 22.2 A 45-year-old patient who initially presented with high-grade osteosarcoma of the fibula. (A) Following neoadjuvant chemotherapy the patient underwent intercalary fibular resection. Approximately a year after the surgery the patient presented with a rapidly enlarging, extensive tumor recurrence. (B) As shown in the MRI, the tumor (arrow) extensively invaded the superficial posterior, deep posterior, and lateral compartments of the leg. Wide excision of the tumor would necessitate removal of the neurovascular bundle and all three compartments. Above-knee amputation was therefore performed.

major bone resection in young patients. Intercalary resection of long bones does not have a major impact on limb length, but resection of the epiphyses does. Since most primary bone sarcomas occur in the second decade of life, after the majority of skeletal maturation has been achieved, and because expandable prostheses are commonly available, amputation for these indications is rare.

CLINICAL CONSIDERATIONS

Staging and Level of Amputation

Patients requiring an above-knee amputation for a soft-tissue or primary bone sarcoma must undergo complete

staging in order to allow the surgeon to determine the level of amputation and extent of soft-tissue resection. The type of flaps to be used is also determined at this time. The combined use of plain radiography, computed tomography (CT), and MRI is necessary to determine the proximal extent of the medullary and extraosseous components of the tumor. In general, the more proximal of the two levels of involvement (i.e. medullary or extraosseous) determines the level of amputation. The level of bone transection should be at least 5–10 cm proximal to this point.

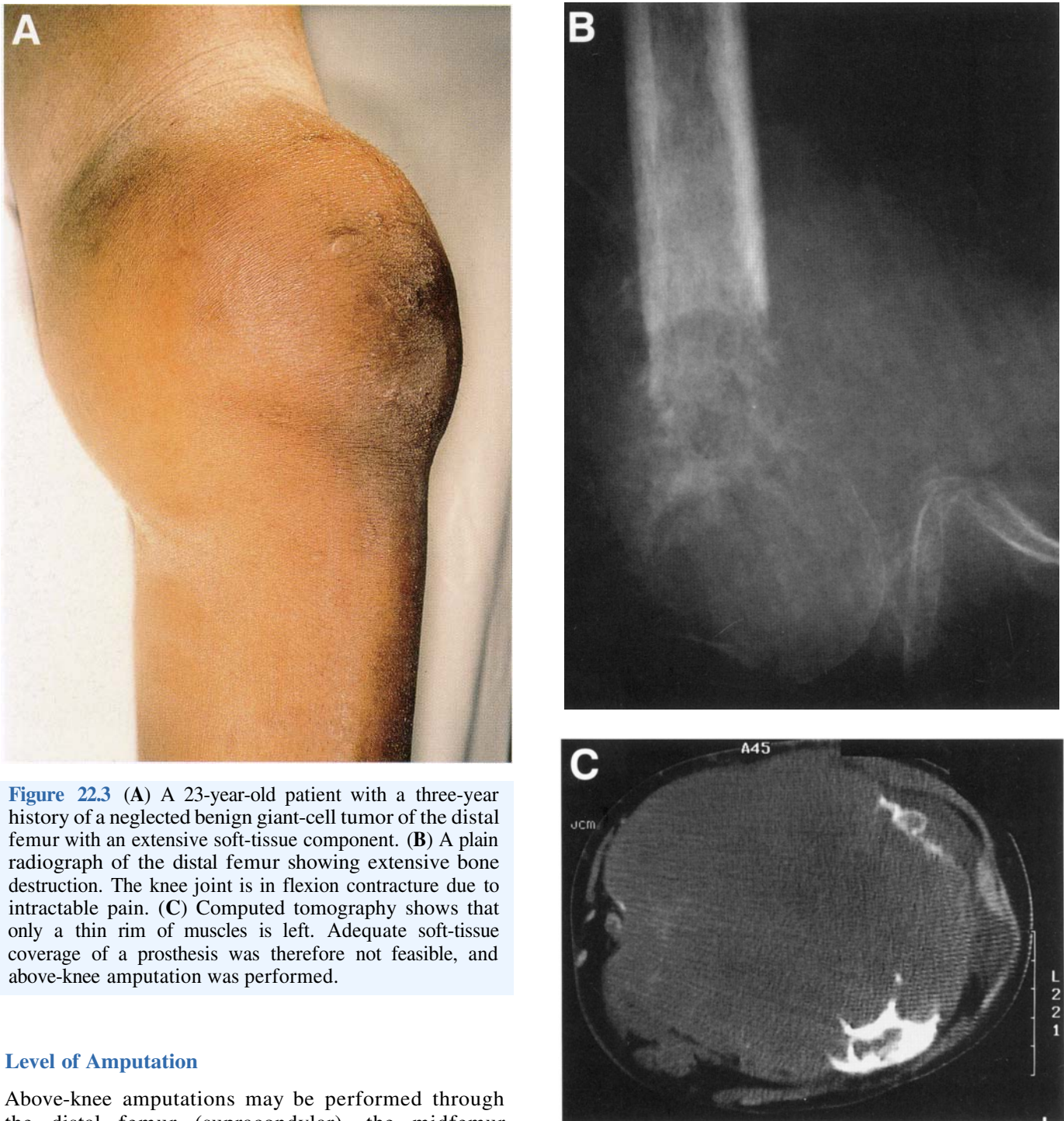


Figure 22.3 (A) A 23-year-old patient with a three-year history of a neglected benign giant-cell tumor of the distal femur with an extensive soft-tissue component. (B) A plain radiograph of the distal femur showing extensive bone destruction. The knee joint is in flexion contracture due to intractable pain. (C) Computed tomography shows that only a thin rim of muscles is left. Adequate soft-tissue coverage of a prosthesis was therefore not feasible, and above-knee amputation was performed.

Level of Amputation

Above-knee amputations may be performed through the distal femur (supracondylar), the midfemur (diaphyseal), or just below the lesser trochanter (high above-knee amputation) (Figure 22.4). Above-knee amputations performed for tumors of the distal femur or sarcomas of the distal thigh tend to be performed at a higher level than standard above-knee amputations. By contrast, tumors of the leg are treated with the standard above-knee amputation. As a rule, any length of femur makes prosthetic fitting easier than none. Even amputations at the subtrochanteric level are preferred

to hip disarticulation; if 3–5 cm of bone distal to the lesser trochanter remain, the patient can be fitted with a prosthesis in a manner used for above-knee amputation.

The main factors that determine the type of flaps to be constructed are the soft-tissue extent of the tumor, areas of prior irradiation, and previous scars. The aim is

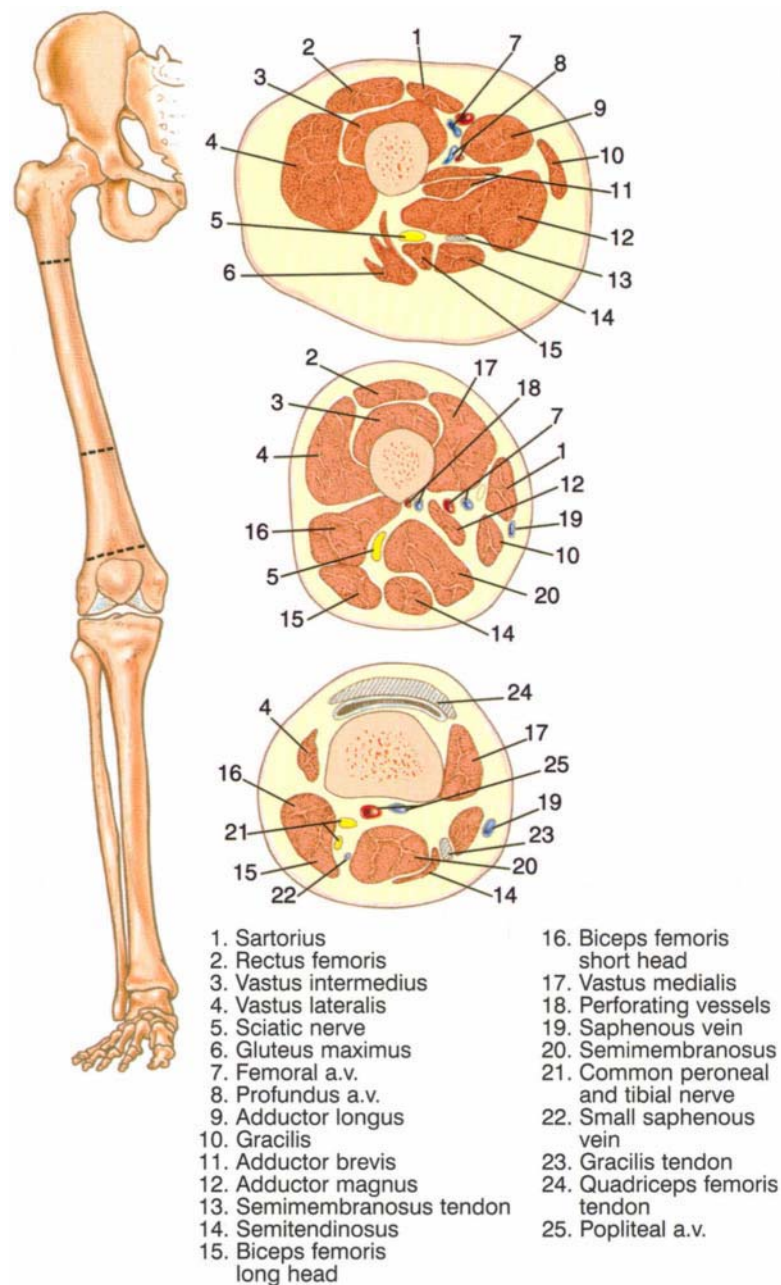


Figure 22.4 Level of osteotomy and cross-sectional anatomy for supracondylar, diaphyseal, and high above-knee amputation. Higher above-knee amputations are generally used for primary bone sarcomas of the distal femur. Low above-knee amputations are used for bone sarcomas of the leg, especially those involving the popliteal fossa or arterial trifurcation. High above-knee amputation is preferable to hip disarticulation, even though the osteotomy is only a few centimeters below the greater trochanter. With the hip joint intact, movement of the prosthesis is greatly facilitated.

to avoid local recurrence and no attempt is made to adhere to standard flaps. At this level a skin or muscle flap of almost any length will heal in the young patient. Furthermore, it is not necessary to use equal flaps; long posterior, anterior, or medial flaps will all heal rapidly.

SURGICAL TECHNIQUE

Figures 22.5–22.12 illustrate the execution of an above-knee amputation. Each step is described in detail. Emphasis is on flap design and meticulous dissection, use of continuous epineural analgesia, myodesis of the major muscle groups to the distal femur, meticulous wound closure, and application of a rigid dressing.

The patient is supine, and the operated extremity should be abducted and flexed (Figure 22.5). Most amputations are performed without compressive tourniquet because it is easier to locate the bleeding edges of blood vessels and perform an adequate hemostasis under such circumstances. The most common type of flap is the anterior and posterior "fish-mouth" flap, and the skin incision should be planned accordingly (Figure 22.6). It is recommended to draw the incision line prior to surgery.

Transection of muscle and bone is shown in Figure 22.7. Major muscle groups should be carefully dissected and tacked for their further use in soft-tissue reconstruction. The femoral edge should be beveled and smooth (Figure 22.8). Cytologic examination and a frozen section of the proximal marrow canal must be performed to ascertain that there is no occult medullary extension of the tumor. A frozen section of any questionable site should be performed.

Sciatic and Femoral Nerves

The cut ends of the nerves may form neuromata, which can be extremely painful when exposed to pressure from the prosthesis or direct trauma. Therefore, the nerve endings must be positioned, and even sutured, within adjacent muscle substance. Malawer *et al.*² described the use of continuous infusion of bupivacaine into the epineural space to control postoperative pain. That method was found to significantly reduce the need for intravenous and oral narcotics, and it is now routinely used in limb-sparing resections and amputations. As shown in Figure 22.9, the epineural catheter is placed under the nerve sheath, in the epineural space. The catheter is sutured to the nerve sheath, pulled through a muscle flap, and secured to the skin. A bolus of 10 ml of bupivacaine 0.25% is injected into the epineural space, and an additional 10 ml are given before the patient leaves the operating room. This is followed by a continuous infusion of 4 ml/h. Boluses of 10 ml can be given as required. The epineural catheter is generally removed after 5 days of treatment, following gradual weaning.

Muscle Reconstruction

Muscle reconstruction around the femur is essential to ensure a functional extremity. In addition, the bone end must be adequately covered and padded with muscles in order to avoid pressure from the prosthesis. The quadriceps and the hamstrings are tenodesed to each other by covering the bone end (Figure 22.10). The hip flexors are stronger than the extensors; thus, the ham-

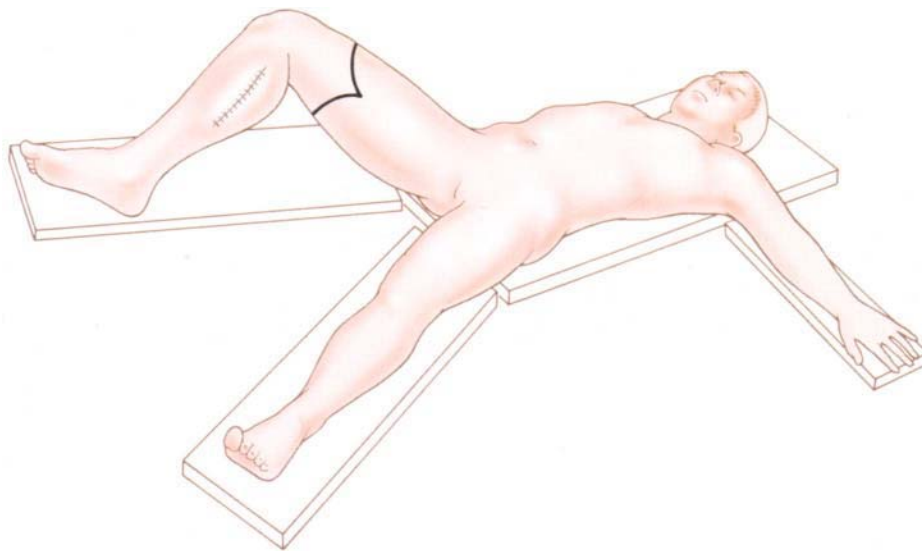


Figure 22.5 Position. The patient is supine; the operated extremity is in flexion and abduction.

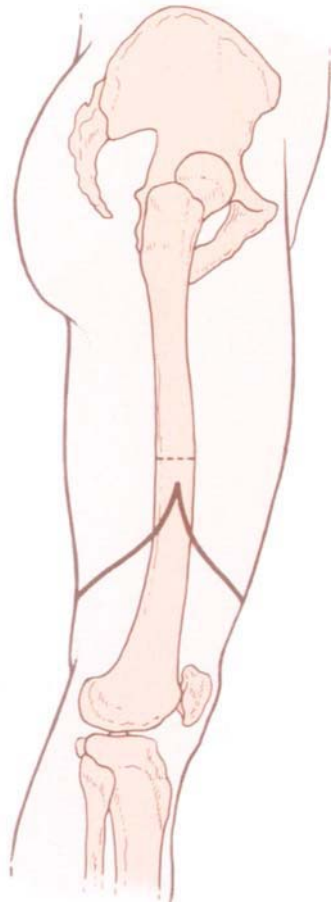


Figure 22.6 Incision. The skin flaps are marked. The main factors that determine the type of flaps are the extent of the soft-tissue tumor, areas of prior radiation, and previous scars. The greatest priority is to avoid local recurrence and no attempt is made to adhere to standard flaps; at this level a skin or muscle flap of almost any length will heal primarily in a young patient. It is not necessary to utilize equal flaps; long posterior, anterior, and medial flaps will heal.

strings should be cut longer than the quadriceps and attached to one another, with the hamstrings somewhat tighter. In addition, the adductors should be tenodesed to these muscles and the femoral stump using drill holes and 3 mm Dacron tapes. This is especially important in the short proximal femoral stump, which has a tendency to go into flexion and abduction.

Closed suction drains are brought out of the medial and lateral aspects of the incision, and the superficial fascia is tightly closed (Figure 22.11). Special attention should be given to wound closure; it is important to avoid large folds of skin. Skin sutures must be positioned by halving the incision, especially if unusual skin flaps have been utilized.

As soon as the surgery is completed, a rigid dressing is applied (Figure 22.12); it is used to reduce the swelling and, if positioned proximally enough, prevent flexion contracture around the hip joint. Contractures are more common with short stumps; to prevent this problem the cast should be continued up to the groin and held in place with a belt. With early ambulation, patients tend to have less pain and experience fewer psychological difficulties. Patients with a rigid cast invariably mobilize earlier than those who have a standard soft dressing. Preoperative or early postoperative chemotherapy is not a contraindication to a rigid dressing and early ambulation. Drains are usually removed on the third or fourth day after the surgery or when each drains less than 50 ml/day. The patient should keep compression on the stump at all times; this is best accomplished with an elastic stump shrinker. As soon as the wound is healed and the stump is not significantly swollen (usually around 4 weeks after surgery), the patient can have the first prosthetic fitting.

REHABILITATION

Successful rehabilitation of the patient who has undergone an above-knee amputation requires a coordinated effort that should start at the time of the staging studies. The health-care team must develop an honest relationship with the patient and family and include them in the decision-making process from the very beginning. Building upon this basis the patient will be better able to accept the amputation and set realistic goals for recovery. The patient should be told that phantom limb sensations might occur following surgery. These sensations should be presented as a normal part of the recovery process. Phantom limb pain is generally controlled by the judicious use of analgesics and the passage of time.

The requirements of above-knee amputees are somewhat different from those of below-knee amputees. Their energy requirements are almost 100% greater, and it is not unusual for the above-knee amputee to require an assistive device (i.e. a cane) for community ambulation, and be less able to participate in sports than a patient who has undergone below-knee amputation. Younger and motivated patients can have a good functional outcome, but older patients can find the energy cost difficult to overcome.

The first stage of recovery is dedicated to proper wound healing and conditioning of the stump. Prevention of flexion contracture of the hip can be achieved with rigid dressing, prone positioning, a physical therapy program and, in most cases, a combination of all three modalities. The use of immediate postoperative prosthesis is more practical and better

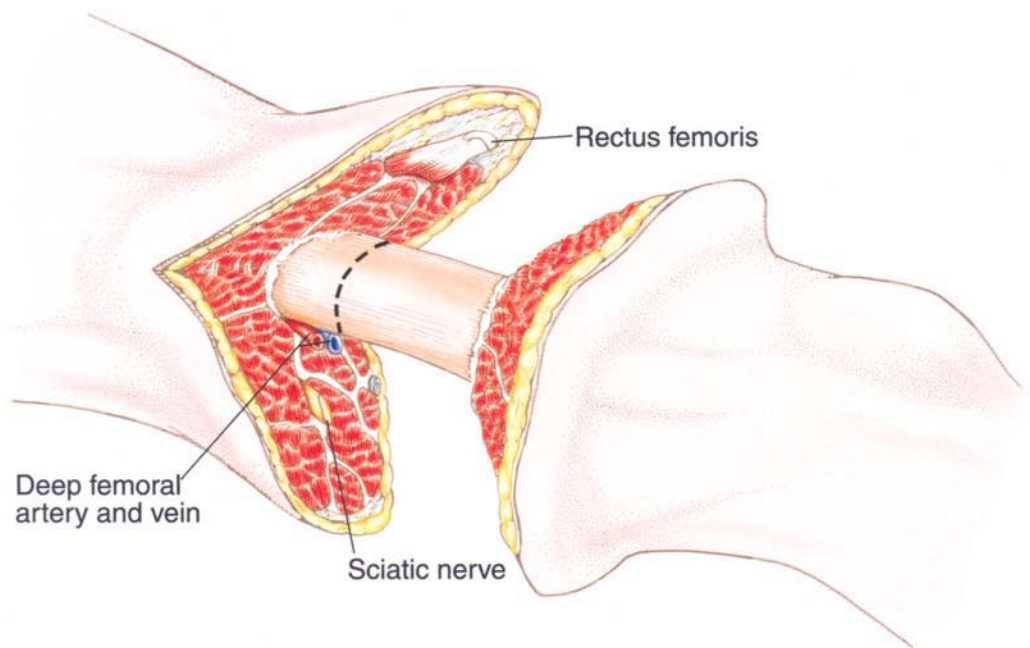


Figure 22.7 Transection of muscle and bone. Incision is performed through the skin, superficial fascia, and subcutaneous tissue vertical to the skin edges. Using electrocautery, muscles are beveled in their transection down to bone. Large vessels are dissected, suture-ligated in continuity, and transected in a bloodless fashion. Nerves should be gently pulled down from their muscular bed approximately 2 cm, ligated with nonabsorbable monofilament sutures, transected with a knife and allowed to retract back to the muscle mass. The bone is transected with an oscillating or Gigli saw without traumatizing the soft tissues.

tolerated by these patients than by below-knee amputees. A temporary prosthesis provides the patient the advantage of training with a simple and adaptable device. It also becomes a backup to the permanent prosthesis, which is fabricated when the residual limb has stabilized in volume and matured to allow full-time wear. Two critical elements are selection of the knee

joint mechanism and suspension system. Many designs, with varying degrees of durability, gait parameters, weight, and stability, are available. Selection of an appropriate product is dependent on patient-specific factors such as age, weight, type of daily activities, and desired sports activities, and requires close consultation with the prosthesist.

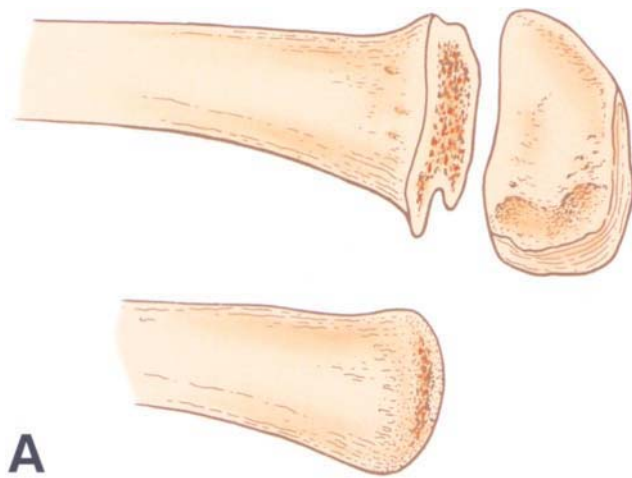


Figure 22.8 (A) The femoral edge should be beveled and smooth. (B) A sharp edge can become extremely painful, especially when pressure from a prosthesis is applied.

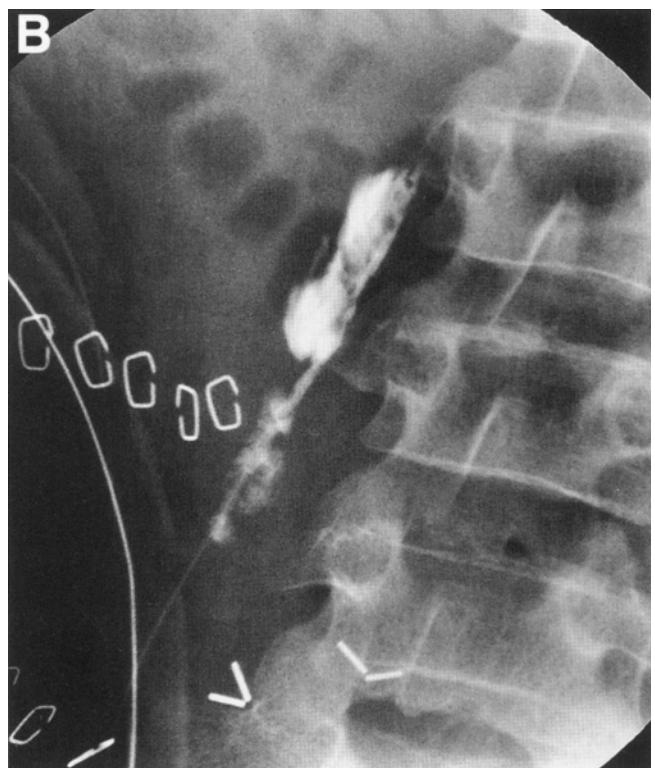
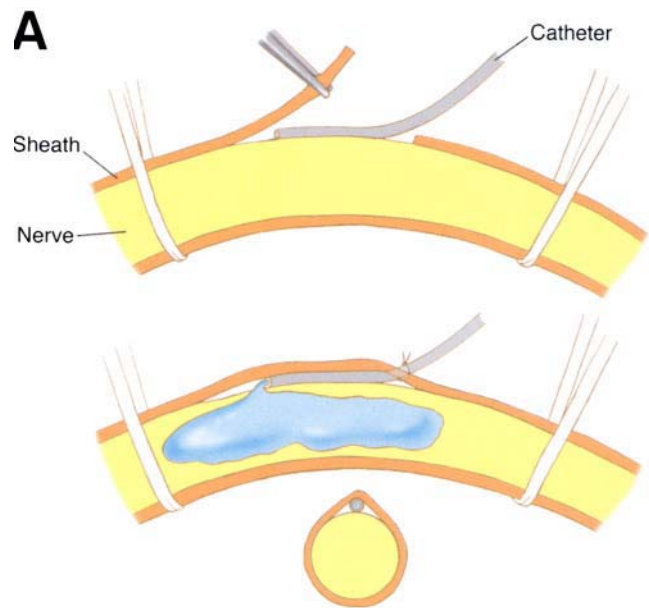


Figure 22.9 (A) Epineural catheter, flushed with bupivacaine 0.25%, is introduced into the epineural space. The catheter is advanced 5–7 cm proximally, and the neural sheath is sutured over the catheter with absorbable sutures. (B) Epineural catheter in the femoral nerve. Contrast dye bolus was injected to demonstrate the distribution of local anesthetics within the epineural space.

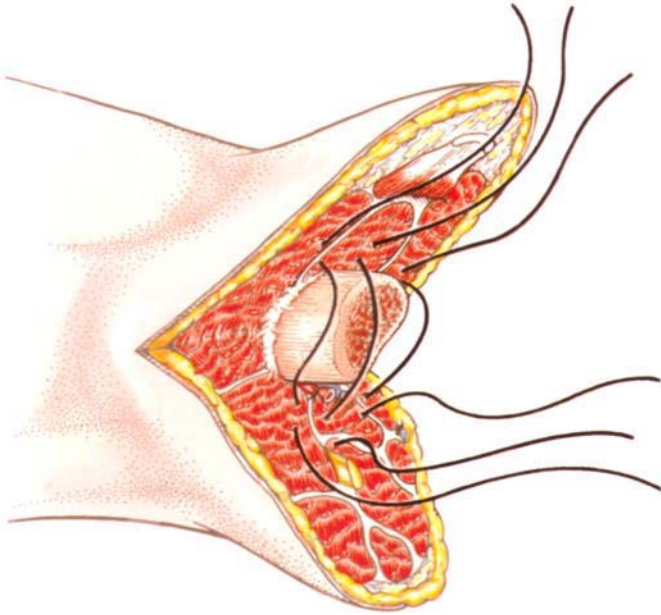


Figure 22.10 A two-layer myodesis is used over the end of the femur. Muscle stabilization of the femur is essential if strength of the limb is to be retained. The quadriceps and hamstrings muscles are myodesed to each other in covering the bony end of the femur, and the adductors are tenodesed to these muscles and the femoral stump using drill holes. This is especially important if there is a short proximal femoral stump, which has a tendency to go into flexion and abduction.

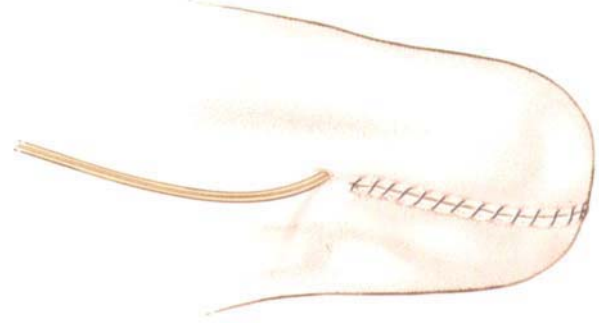


Figure 22.11 Closed suction drains are brought out of the medial and lateral aspects of the incision. It is important not to stitch these catheters to the skin, because they will be removed from inside the rigid dressing.



Figure 22.12 Application of a rigid dressing.

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Below-knee Amputation

Martin Malawer, Jacob Bickels and Paul Sugarbaker

OVERVIEW

Below-knee amputation is usually performed for extensive high-grade soft-tissue sarcomas of the lower leg, ankle or foot. Primary bone sarcomas rarely occur in these locations. Extensive infiltration of tendons and ligaments and around bones in this area may preclude a functional extremity following wide excision. The almost universally good functional outcome of below-knee amputation makes it an even more realistic option. General considerations that were discussed for above-knee amputation also apply for below-knee amputation; design of skin flaps is determined by the anatomic extent of the individual tumor and the large majority of these patients heal uneventfully. Emphasis is on flap design and meticulous dissection, use of continuous epineural analgesia, myodesis of the major muscle groups of the distal tibia, meticulous wound closure, and application of a rigid dressing.

INTRODUCTION

Below-knee amputation was traditionally performed for malignant tumors of the ankle and foot (Figure 23.1). In recent years, improvements in preoperative chemotherapy and adjuvant radiation therapy have led to better local tumor control and allowed the execution of limb-sparing surgery in the majority of these cases. Still, approximately 20–25% of these tumors are treated with an amputation. This rate, which is much higher than the 5–10% amputation rate for tumors around the knee, stems from two significant anatomic–biological differences between the two locations. First, there are no true anatomic compartments around the ankle and foot. The lack of thick fascial septa and anatomic compartments results in wide spread of any tissue pathology that otherwise would be confined to a narrower space. Second, the anatomic distance between functional compartments (i.e. flexor and extensor tendons and muscles) is short, and most extensive tumors violate both compartments. These two facts explain why tumors of the ankle and foot grow diffusely and cross different regions of the foot early in their growth, and why wide excision usually results in a severe loss of function.

There are no strict guidelines, indications, or contraindications for below-knee amputations; decisions are made on a case-by-case basis. As with any other amputation, all patients are evaluated for a limb-sparing surgery, and amputation is performed only when this option has been ruled out. General indications for below-knee amputation are extensive, infiltrative high-grade sarcomas of the lower extremities (Figure 23.2), extensive involvement of the lower leg with bone sarcoma (Figure 23.3), or recurrent disease that lacks a local excision option (Figure 23.4). In these cases, negative margins cannot be attained without extensive removal of tendons, muscles, nerves, and other anatomic structures that provide function to the lower extremity. Major vascular or nerve involvement, however, is rarely an indication for an amputation, because at that distal point of the extremity, vascular and nerve structures are widely separated by bony structures. Rarely will amputation be initially performed for a low-grade tumor. The efficacy of adjuvant radiotherapy allows one to perform marginal excision of these tumors, which are unlikely to result in metastatic disease.

PREOPERATIVE EVALUATION

Complete staging studies are performed as described in Chapter 22. A preoperative consultation with a prosthetist and rehabilitation specialist, as well as a psychologist who is familiar with these patients, is extremely useful. The purpose of these sessions is to



Figure 23.1 Below-knee amputation is performed for malignant tumors of the distal leg, ankle, and foot.

describe to the patient the various stages of recovery and the expected functional outcome. In addition, a meeting between the patient and a below-knee amputee from the same age group, and with the same underlying disease, is very encouraging. Because of the elective nature of these procedures, it is usually not difficult to arrange these consultations.

SURGICAL TECHNIQUE

The level of below-knee amputation in patients with primary bone sarcomas of the distal leg must be carefully determined. Below-knee amputation has to achieve

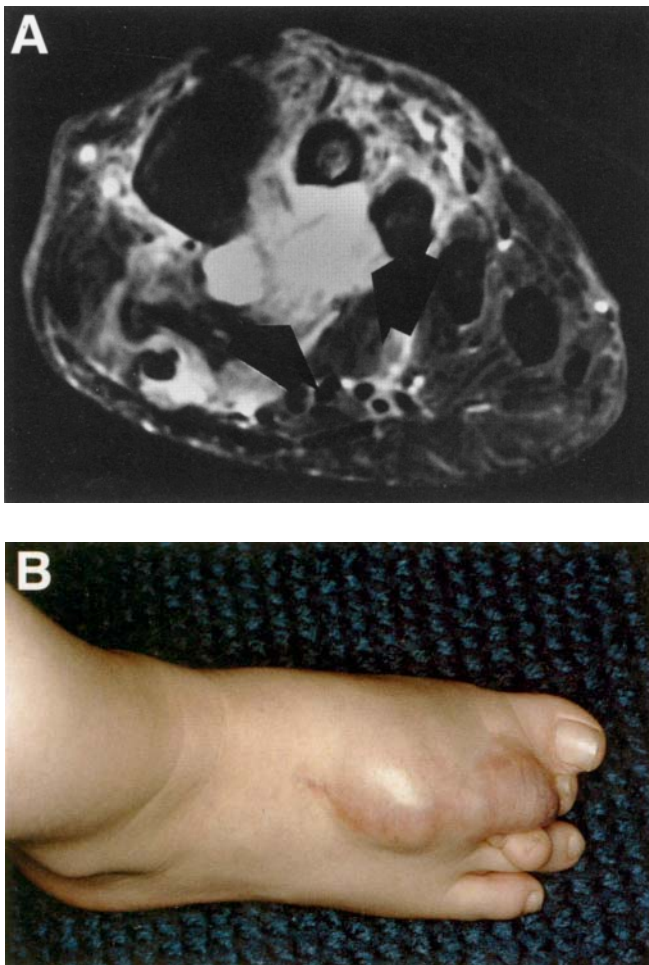


Figure 23.2 (A) T2-weighted magnetic resonance image of the foot, showing extensive high-grade malignant fibrous histiocytoma (MFH) (arrows) of almost the entire plantar aspect of the foot. Extension to the dorsal aspect of the foot is noted. (B) Extensive high-grade angiosarcoma of the dorsal aspect of the foot.

wide margins, and the medullary and extraosseous extent of the disease must therefore be evaluated. If necessary, amputation at a higher level must be performed. A good outcome generally requires that the limb be of adequate length, i.e. at least 3 cm below the tibial tuberosity. It also requires good soft-tissue coverage and a rounded contour of the distal end of the tibia with a residual fibula several centimeters shorter (Figure 23.5). As a rule, the longer the stump, the better the functional outcome. Because the majority of tibial elongation during skeletal maturation stems from the proximal tibia, almost any level of below-knee amputation is acceptable in a child. With growth, a functional stump will be obtained, and adaptation of the patient is generally excellent. High below-knee amputation is

acceptable for tumors below the level of the musculotendinous portion of the gastrocnemius muscles.

Figures 23.6–23.10 illustrate the execution of below-knee amputation and provide a detailed explanation of each step. Emphasis is on flap design, use of continuous epineural analgesia, myodesis of the major muscle groups of the distal tibia, meticulous wound closure, and application of a rigid dressing.

Because of the subcutaneous location of the tibia and the relatively small volume of muscle in the anterior compartment of the leg, the authors prefer to use a long posterior flap, rather than the classic “fish-mouth” flaps. Amputations, especially in young patients, can be extremely painful; for this reason the installation of an epineural catheter and the use of continuous epineural analgesia are strongly recommended. The authors have extensive experience and excellent results with this modality, the technique of which was described in Chapter 22.

Functional myodesis of the major muscle groups of leg to the distal tibia will provide excellent soft-tissue coverage to the stump and allow an adequate range of motion of the knee joint. To help prevent wound-healing problems resulting from preoperative chemotherapy, and avoid any delay in administration of radiation therapy or postoperative chemotherapy, wound closure must be meticulous. Hematomas and seromas must be avoided by the use of adequate closed-suction drainage and the application of a rigid dressing.

REHABILITATION

Successful rehabilitation of a below-knee amputee requires a coordinated, multidisciplinary effort. It may take up to 6 months before the definitive prosthesis can be fitted. There are three stages in the recovery process. The goal of the first stage is to ensure optimal wound healing and conditioning of the residual limb through physical therapy in order to prepare it to accommodate the stress of the prosthesis. A special “stump-shrinker” sock is used to decrease the swelling, and a simple knee immobilizer or custom splint is used to avoid the development of a flexion contracture around the knee joint. The use of a removable splint allows participation in physical therapy, protection from contusion, and easy inspection of the wound. The use of an immediate postoperative prosthesis carries high risk with little gain; i.e. the risks of wound problems and pain-management difficulties outweigh the psychological benefits.

The second stage begins when the wound has healed and the residual limb is nontender and able to withstand the stress of a temporary prosthesis. This stage is dedicated to gradually increasing wear time and enables the patient to tolerate the prosthesis-

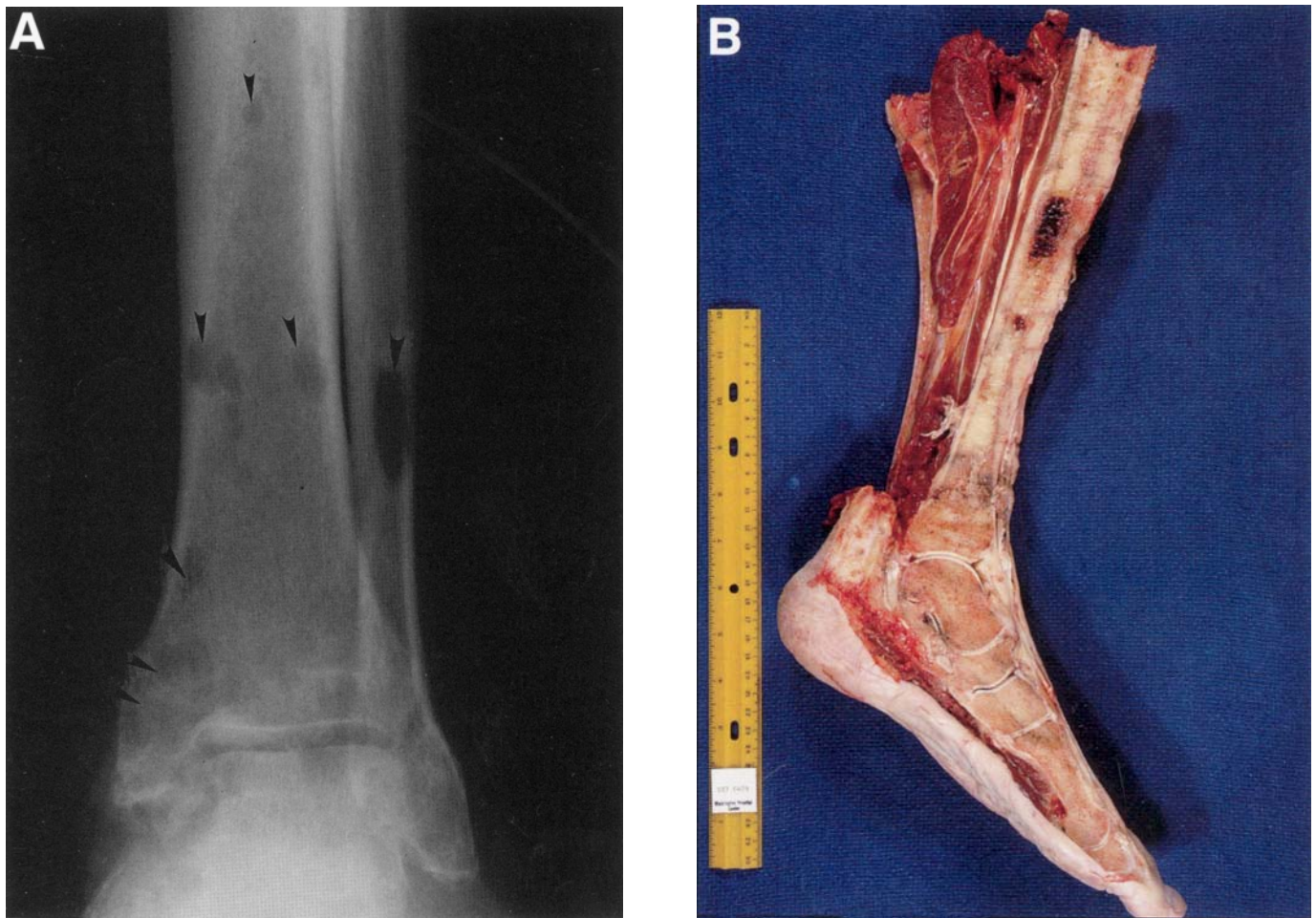


Figure 23.3 (A) Angiosarcomatosis of the leg and foot. Note the multiple lytic lesions of the distal third of the tibia, fibula, and talus (arrows). (B) Sagittal cut of the surgical specimen. The entire tibial medulla is occupied by the tumor. Note the anterior cortical breakthrough and soft-tissue extension.



Figure 23.4 (left) Locally recurrent carcinoma (arrows) of the foot. This local recurrence, the patient's fifth, occurred only a few months following the previous resection within the irradiated field.

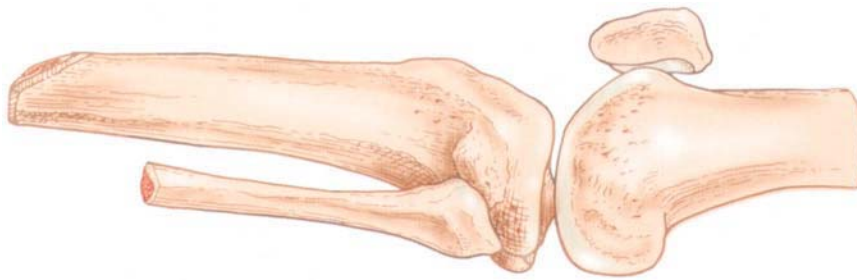


Figure 23.5 Osteotomy of the tibia and fibula. The longer the stump, the better the functional outcome. We routinely resect the fibula several centimeters proximal to the tibial osteotomy in order to construct a tapered and beveled stump.

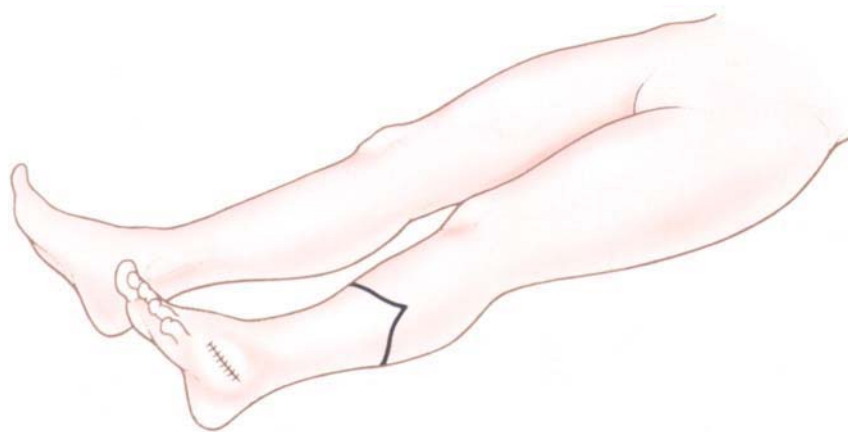


Figure 23.6 Position and incision. The patient is supine on the operating table with slight elevation of the operated extremity. The skin incision is carefully marked out to provide well-vascularized and nonirradiated skin, as well as an underlying bulk of muscle tissue for coverage of the stump.

related stress on the residual limb. The patient wears the stump-shrinker sock whenever the prosthesis is not being worn. This prevents changes in the volume of the residual limb due to dependency, which might lead to prosthetic fit problems and pain. The second stage may last from 3 to 6 months. It ends when the patient is able to wear the prosthesis all day without pain and significant changes in the volume of the stump. Fitting

of the definitive prosthesis, which is the third stage, takes place at that point. Premature efforts to fit the prosthesis will often require fabrication of a new socket because of volume changes in the residual limb. Selection of the components of the definitive prosthesis is dependent on patient-specific factors such as age, weight, type of daily activities, and desired sport activities.

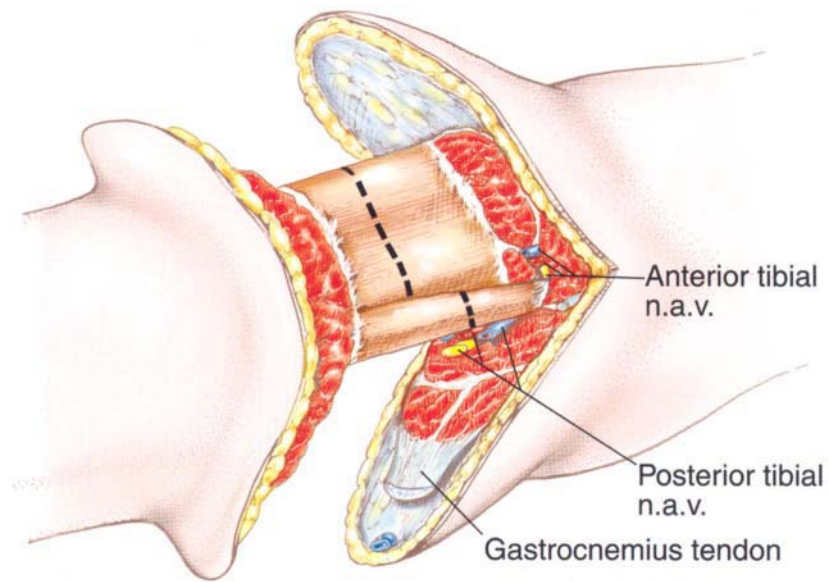


Figure 23.7 Soft-tissue dissection and bone transection. The skin, superficial fascia, and subcutaneous tissue are cut perpendicular to the skin surface. The muscles are transected with electrocautery. Vascular structures are ligated in continuity and divided. Major blood vessels are suture-ligated. Nerves are meticulously dissected and gently pulled 2 cm out of their surrounding muscle mass. They are double-ligated with monofilament nonabsorbable suture. The large muscle groups are tapered so that they can be secured over the cut ends of the bone. Osteotomy of the tibia is shown in [Figure 23.5](#). If the amputation is performed for a primary bone sarcoma, intramedullary content from the edge of the stump should be sent for frozen section to verify that it is free of tumor. If the amputation is performed for a soft-tissue sarcoma, soft tissues from the surgical margins should be assessed in a similar manner. Following transection, the tibial edge should be beveled. As discussed in Chapter 22, the use of continuous epineural analgesia is highly recommended.

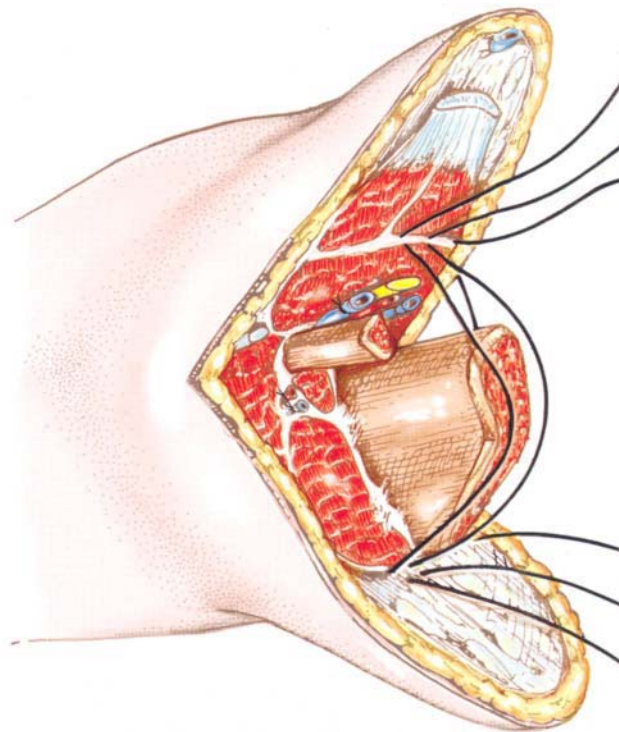


Figure 23.8 Myodesis over the distal tibia. Using drill holes in the distal tibia, the major muscle groups are attached to the bone with heavy sutures. Muscle layers are closed over the entire circumference of the bony stump.

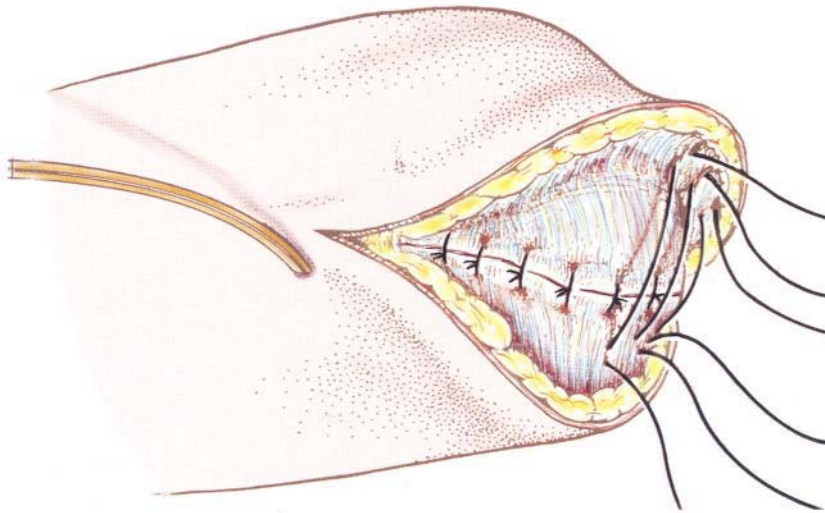


Figure 23.9 Closure of superficial fascia and skin over suction drains. It is important that the superficial fascia be meticulously closed. Skin flaps should be closed without any remaining skinfolds. Closed-suction drains are placed. These should not be sutured in place because they will be removed from beneath the rigid dressing within a few days.

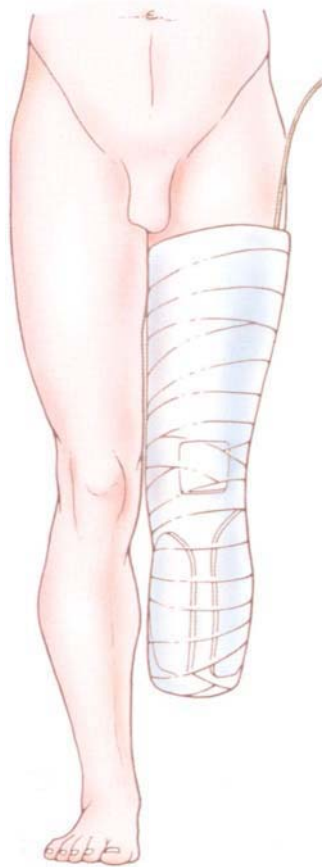


Figure 23.10 A rigid dressing is used in the early postoperative period to reduce swelling and prevent flexion contracture. Early ambulation is begun in most patients.

Phantom Limb Pain

Lee Ann Rhodes

OVERVIEW

Phantom limb pain can be a devastating consequence of an amputation. It is often a chronic, disabling condition. This chapter reviews the etiology, pathophysiology, prevention, and treatment of phantom limb pain and discusses known risk factors for this condition. Even though many physicians have been frustrated by the inability to control phantom limb pain, promising new therapies are on the horizon.

CLINICAL PRESENTATION

Nearly every man who loses a limb carries about with him a constant or inconstant phantom of the missing member, a sensory ghost of that much of himself. The sensation of the presence of the part removed exists in many persons as soon as they come from under the influence of the anaesthetic used at the time of the amputation, but in others it only arises after they cease to suffer pain, rarely delayed beyond three weeks. (S. Weir Mitchell¹)

It has been more than a century since Mitchell published his detailed observations about Civil War amputees. Mitchell distinguished several categories of post-amputation phenomena. These categories have become known as phantom limb pain, phantom sensations, stump pain and super-added phantom sensations. Phantom limb pain is a noxious sensation where the limb existed.²⁻⁵ Phantom sensations are nonpainful sensations of the missing limb.³ Stump pain is pain that is restricted to the amputated site.⁴ Super-added phantom sensation describes the sensation of an object, such as a wrist watch or ring, attached to the phantom limb.⁴

Most people with phantom limb pain experience more than one type of pain. Sherman⁶ distinguished three major types of pain: lacerating, cramping, and burning. Other types of pain may be sharp; pins-and-needles sensations, itching, pinching, stinging, aching, crushing, twisting, and grinding.³ The pain typically occurs in the distal region of the phantom limb.⁷ The distribution of the pain rarely follows the path of the severed nerve.² The pain is often constant and many amputees report having intermittent pain exacerbation.

Patients may report that the phantom limb is in an awkward position, or that it feels as if it were moving either spontaneously or voluntarily.^{6,8} The phantom limb may feel so real that an amputee may attempt to reach for objects with the phantom hand or try to step with the phantom foot.⁹ In addition, most amputees experience a sense of the length and volume of the missing limb.⁸

The phantom limb may develop a phenomenon called telescoping.⁴ This is most often seen in those with painless phantom limbs, and usually occurs within the first year after amputation. As telescoping occurs, the middle portion of the phantom limb is perceived to be shortened while the most highly innervated area, such as a hand or foot, feels as though it is attached close to or directly on the stump.¹⁰ Telescoping occurs more often in the upper than in the lower extremity. With time, amputees may experience the sensation of a markedly shortened phantom limb. The last sensations to disappear are those that have the highest

representation in the cortex, such as the index finger, thumb, and great toe.³

The existence of the phantom limb may be strengthened by sensations that resemble feelings in the limb that existed prior to the amputation.¹¹ This phenomenon is termed somatosensory memory^{12,13} and may include pains from injury to soft tissues, bones, or joints or other pains that were experienced prior to the amputation.^{14,15} For example, pain may be continued from a foot ulceration that was present in the limb prior to amputation.¹¹ In a further exploration of this concept, Katz and Melzack¹⁴ found 57% of patients who had an amputation as a result of ischemic vascular disease or trauma reported that pain in the phantom limb was similar in location and quality to that experienced in the limb itself prior to amputation; this rate was only 12.5% in patients who had undergone amputation because of a malignancy.

EPIDEMIOLOGY

Phantom limb pain was once thought to be quite rare; most likely because of the patients' reluctance to mention the pain because of fear of ridicule.³ Many reports have been published regarding the incidence of phantom pain.¹⁶⁻¹⁹ In a survey of 590 veteran amputees, 55% reported phantom pain and 56% reported stump pain.¹⁶ Sherman⁶ found that 70% of amputees reported phantom limb pain within the first 2 years following amputation. Up to 88% of patients undergoing hip disarticulation or hemipelvectomy suffer from phantom limb pain.¹⁸ This supports Roth and Sugarbaker's¹⁹ finding that the higher the level of lower extremity amputation, the greater the incidence of moderate to severe pain.

Phantom limb pain occurs soon after amputation and can be long-lasting.²⁰ Jensen *et al.*¹⁰ found that phantom limb pain occurred within 8 days after amputation in 72% of adult patients. Nikolajsen *et al.*¹⁵ observed that the incidence of phantom pain did not decrease 6 months following amputation, although there was a decrease in the duration of their intermittent pain exacerbations. In 3–10% of amputees the pain is chronic and severe.¹⁶

Although many children experience phantom sensations, the incidence of phantom limb pain is lower in the pediatric population than in adults.²¹ In a retrospective study of 75 pediatric patients, 48% of those with amputations necessitated by cancer and 12% of those who had traumatic amputations reported phantom limb pain.²² Melzack *et al.*²³ studied a group of pediatric patients who had either a congenital limb deficiency or an amputation before the age of 6 years. Phantom limb sensations were present in 20% of

congenitally limb-deficient subjects and in 50% of those who had undergone amputations before the age of 6. The presence of pain was 20% in the congenital limb-deficient group compared to 42% in the young amputees. Some of the differences between the adults and children may be attributed to under-reporting of pediatric pain.²¹ A pediatric study surveying children age 5–19 years who had had an amputation within the previous 10 years found 92% reported pain, although this was reflected in only 50% of the patients' medical records.²¹

In the Melzack *et al.* study,²³ 42% of pediatric amputees developed phantom sensation with a mean onset of 2.3 years. Thirty-five percent of children have resolution of their phantom pain within 10 years of their amputation.²¹ Sixty-seven percent of pediatric patients also had a decrease in their phantom sensations, while 14% actually were found to have an increase in their phantom sensations, over a 10-year period.²¹

ETIOLOGY

Preamputation pain is a risk factor in the development of phantom pain following amputation.¹⁰ Even pain that had been experienced in the limb months or years before amputation can be re-experienced as phantom pain.

Nikolajsen *et al.*¹⁵ found that a preamputation pain score greater than 20 mm on the visual analogue scale was associated with an increased risk of phantom pain, but the duration of preamputation pain did not appear to be related to the intensity of phantom pain. The visual analog scale is a 100 mm line with no pain located to the left (0 mm) and worst pain imaginable being to the right (100 mm).¹⁵ Although the incidence of mental illness in patients who develop phantom limb pain is no greater than in those who do not, stress, anxiety, dysphoric mood, and emotional triggers may contribute to the persistence or exacerbation of phantom pain.^{6,24–26}

Another factor that may be associated with phantom pain is chemotherapy, especially those agents known to cause peripheral neurotoxicity.^{22,27} In a study of pediatric amputees the incidence of phantom limb pain was 74% in patients who had received chemotherapy (either vincristine or cisplatin) prior to amputation. This was reduced to 44% in patients who began chemotherapy after their limb surgery, although all four patients in the postamputation chemotherapy group developed pain within 72 h of the chemotherapy.²² Phantom limb pain developed in only 12% of patients who never received chemotherapy.²² It remains unclear whether or not this is also true in adult

amputees who have received these chemotherapy agents.

Reappearance of quiescent phantom pain has been reported during spinal anesthesia^{28,29} and epidural anesthesia with local anesthetics.^{5,30} The pain begins as the block recedes.³¹ Although the incidence of rekindling phantom limb pain during spinal anesthesia is quite low (about 5%), it can be severe and difficult to treat.^{32–34} Phantom limb pain may also be exacerbated by metastatic disease^{3,35} or tumor recurrence.³⁶ There is a case report of exacerbation of phantom limb pain following magnetic resonance imaging.³⁷

PATHOPHYSIOLOGY

It is now widely accepted that phantom limb pain is the result of complex interactions between the peripheral and central nervous systems. At the time of amputation, severing of the peripheral nerves disrupts normal afferent nerve input into the spinal cord. This process, often referred to as deafferentation, results in the degeneration of the distal portion of the peripheral nerves; the proximal portion, however, survives.^{7,38}

Subsequently, abnormal discharges develop in the sprouts, known as neuromas, of the regenerating proximal nerves.^{39,40} These ectopic abnormal discharges are the result of increased excitability in the sprout, which occurs because of the accumulation of transported chemical mediators. These mediators accumulate in the neuroma following anterograde axoplasmic transport from the cell body to its periphery.⁷ Increased firing occurs in the neuroma as it becomes hypersensitive to mechanical, chemical, and metabolic changes.⁷

Peripheral mechanisms do not totally explain the phenomenon of phantom limb pain because conduction blockade of the peripheral nerves usually does not eliminate it.⁴⁰ In addition, even if the ectopic discharges resolve spontaneously, surgically, or as a result of pharmacotherapy, phantom limb pain usually persists.⁷ This may be because abnormal c-fiber afferent activity, that starts after the amputation of the peripheral nerve, leads to changes in the spinal cord itself.⁸ Reorganization occurs in the receptive fields of the spinal cord. New synaptic connections form from the axonal sprouting of the proximal section of the amputated peripheral nerve. In areas of the spinal cord that are not responsible for the transmission of pain, some axons that previously terminated begin to sprout into lamina II of the dorsal horn. This lamina is the region that is typically involved in the transmission of painful nociceptive afferent inputs.⁷ The dorsal horn of the spinal cord also starts exhibiting central hyperexcitability, as demonstrated by an increased rate of

firing. This process, referred to as the wind-up phenomenon, is mediated by substance P, tachykinins, and neurokinin A's action at the *N*-methyl-D-aspartate (NMDA) receptor, with concomitant up-regulation of the receptors.^{7,8} At the same time that the excitability of the dorsal horn of the spinal cord occurs, there is a decrease in the normal inhibitory interneuron activity.^{38,40} This interplay leads to the increased transmission of pain signals.

Changes occur not only in the peripheral nervous system and spinal cord but also in the cerebral cortex. It is hypothesized that amputees retain neural activity and function of the thalamic representation of the amputated limb. Evidence in support of this theory has been found during functional stereotactic mapping; microstimulation of certain areas of the ventrocaudal thalamus in amputees produces painful sensations in the phantom limb.⁴¹ In addition, the representation in the thalamus of the stump area increases in some amputees.

This is consistent with the findings of animal studies in which there is enlargement of somatotopically adjacent areas into the deafferented regions.⁴¹ This cortical reorganization partly explains some instances in which afferent nociceptive stimulation of neurons within the stump or surrounding areas can produce sensations in the missing limb. This occurs because the region of the cortex that was once responsible for receiving input from the amputated limb is now processing information from the stump and referring the sensation to the phantom limb.⁴²⁻⁴⁴

The amount of cortical reorganization appears to be directly proportional to the degree of pain.⁴³ When some amputees experience a reduction of phantom limb pain with local anesthetic conduction blockade (e.g. spinal anesthesia used during surgery), they also experience a temporary reduction in the amount of cortical reorganization in the somatosensory cortex.⁴⁵

In addition to the peripheral and central mechanisms involved in the pathophysiology of phantom pain, Melzack^{11,46,47} has described a neuromatrix responsible for phantom limb pain. This matrix is a large, widespread network of neurons that consists of loops between the thalamus and cortex and between the cortex and limbic system.⁴⁶ Melzack proposes that there is a genetically determined central representation of the body image that interacts with cognitive and somatosensory memories of the limb and that it is unique to each person. It is modified by the individual's sensory inputs and gives each person a neurosignature, which is a continuous outflow from the neuromatrix to certain brain areas referred to as the sentient neural hub. This hub converts the flow of neurosignatures into the flow of awareness, resulting in the sensations

experienced by the amputee.⁴⁶ The concept of the neuromatrix allows for contributions of both age-dependent and age-independent experiences of phantom pain and possibly accounts for the lower incidence of phantom limb pain in the pediatric population.⁴⁶

An extension of the neuromatrix theory is that of the phantom limb open-circuit. When an extremity is amputated, the return signal from that limb disappears while the outgoing signal from the neuromatrix remains.⁴⁸ This alteration in signals may be responsible for the perception of phantom limb pain. On the basis of this tenet, phantom limb pain may be decreased by either eliminating the outgoing signal from the neuromatrix or by creating a normal return signal via electrical stimulation.⁴⁸

Canavero⁴⁹ opposes Melzack's neuromatrix theory of phantom pain on the basis of evidence that a focal brain lesion involving the parietal cortex, thalamus, or corticothalamocortical fibers contralateral to the amputated limb can relieve phantom pain. Melzack contends that the neuromatrix is widespread and therefore not amenable to lesioning. Canavero⁴⁹ hypothesizes that prior surgical techniques were inadequate and may some day be used to treat phantom pain. Future work will focus on the selective interruption by bilateral stereotactic lesioning of a local reverberatory loop that sustains phantom limb pain between the sensoricortical area and the thalamus.

PREVENTION

The establishment of analgesia prior to surgical incision (pre-emptive analgesia)⁵⁰ may help control postoperative pain by preventing the transmission of noxious afferent input from the periphery to the spinal cord.⁵¹ Otherwise, a prolonged state of central neural sensitization and hyperexcitability could occur that would amplify future input from the amputated site.⁵² Epidural and epineural analgesia, given preoperatively and postoperatively, have revolutionized the ability to manage pain. With these techniques the need for postoperative opioids, as well as their associated side effects, has decreased. Until recently, epidural analgesia was thought not only to optimally manage postoperative pain following an amputation but also to decrease the incidence of phantom limb pain.⁵³⁻⁵⁵ The validity of these studies, however, is questionable because of small sample sizes and insufficient randomization.⁵⁶ A recent randomized, double-blind, placebo-controlled study by Nikolajsen *et al.*⁵⁶ found that epidural blockade with bupivacaine and morphine did not prevent phantom or stump pain. In this study, epidural analgesia was started at least 15 h

prior to amputation and continued for a minimum of 2 days. The incidence of phantom limb pain and stump pain was the same in the control and epidural groups at 1 week, 3 months, 6 months, and 12 months after the amputation.⁵⁶

Epidural clonidine is now being administered for neuropathic pain. In a prospective, controlled study, 13 patients received epidural infusions containing bupivacaine 75 mg, clonidine 150 μ g, and morphine 5 mg in 60 ml of normal saline. The infusion of 1–4 ml/h was initiated 24–48 h preoperatively and continued for at least 3 days. The control group received IV opioid patient-controlled analgesia. The incidence of phantom limb pain was 8% in the epidural group compared to 73% in the control group.

Side-effects of the epidural infusion were temporary urinary retention and bowel incontinence.⁵⁷ Before any conclusions can be drawn regarding the prevention of phantom limb pain by the addition of clonidine to the epidural bupivacaine and morphine, a larger study, done in a manner similar to that of Nikolajsen *et al.*⁵⁶ is needed.

Postamputation analgesia and prevention of lower extremity phantom limb pain have been investigated using infusions of local anesthetic placed into a nerve sheath via a catheter at the time of amputation.^{58,59} Although regional anesthetic techniques offer many advantages of pain control during the perioperative and postoperative periods, the results of several studies are conflicting. Fisher and Meller⁶⁰ conducted a pilot study of 11 patients undergoing an above- or below-knee amputation with a continuous perineural infusion of 0.25% bupivacaine at 10 ml/h into the sciatic or posterior tibial nerve sheath. The infusion continued for 3 days. Postoperative opioid requirements were significantly lower compared with those of a retrospective control group, given parenteral opioids. None of the patients who received the peripheral nerve infusions developed phantom limb pain during the 12 months of follow-up.⁶⁰ Similar findings were reported by Malawer *et al.*⁵⁹ in a study in which local anesthetic was administered directly into the peripheral nerve sheaths following an amputation (Figure 24.1). When compared with historical controls there was an 80% reduction in narcotic requirement for the 72 h following surgery.⁵⁹

Pinzur *et al.*⁶¹ conducted a randomized controlled study in which a local anesthetic was infused adjacent to the transected nerve but not within the nerve sheath. A sciatic nerve catheter was used for transfemoral amputations, while posterior tibial nerve catheters were used for transtibial amputations. All amputations were done because of ischemic changes secondary to peripheral vascular disease. Bupivacaine 0.5% at 1 ml/h

was used for the local anesthetic infusion. The control group studied received opioids only. In the first two postoperative days, morphine use was lower in the infusion group than in the control group. By the third postoperative day no statistical significance in opioid requirements was present between the two groups. At 3 and 6 months after the amputation there was no difference in the incidence of phantom limb pain between the infusion and control group.⁶¹ It is possible that some of the differences may be attributed to the placement of the catheter adjacent to the nerve ending instead of threading it up the sheath, combined with the low volume (1 ml versus 4–10 ml/h) of local anesthetic given hourly in the Pinzur study compared with that given by Fisher and Meller.⁶²

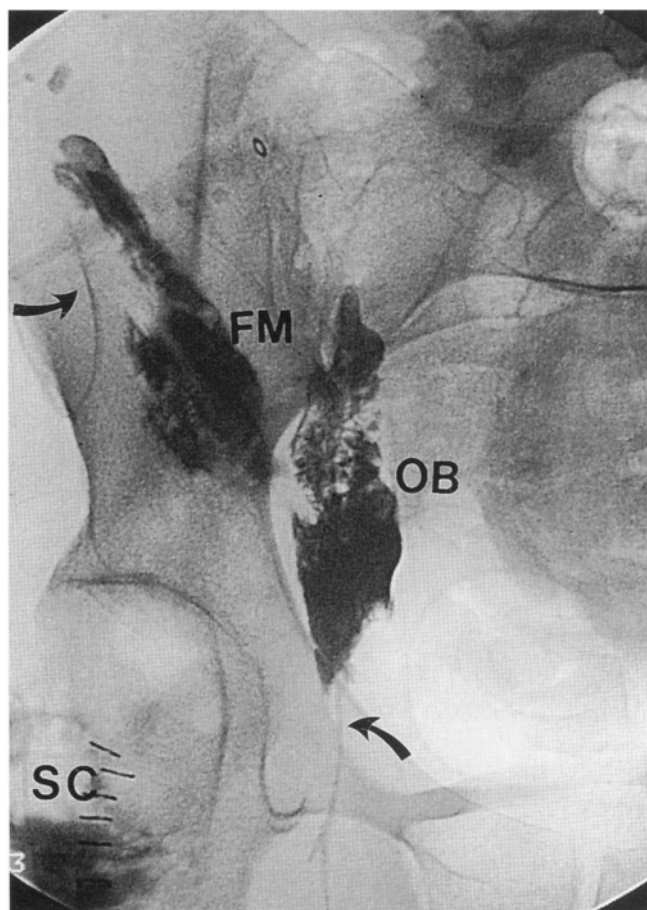


Figure 24.1 Radiograph following a hip disarticulation. Epineural catheters were placed within the nerve sheaths prior to wound closure. Contrast dye was injected to show the distribution of local anesthetics along the nerve sheaths. (SC = sciatic nerve, FM = femoral nerve, OB = obturator nerve). This patient was pain free postoperatively. Epineural catheters are not removed until the 5th postoperative day.

A retrospective, unblinded study of patients who had undergone lower extremity amputations compared the incidence of phantom limb pain in patients receiving a continuous infusion of bupivacaine 0.5% with those receiving only opioids. Bupivacaine at 2–6 ml/h was infused via a catheter into the sciatic or posterior tibial nerve sheath. The catheter was placed under direct supervision during surgery. In the infusion group a bolus of 10–20 ml of 0.5% bupivacaine was given shortly before the end of surgery. The catheters were maintained for 3–7 days. Postoperative opioid requirements and the incidence of phantom limb pain at 6 months were not significantly different between the two groups.⁶³ Two limitations of this study were the use of a heterogeneous group of patients having amputations for a variety of conditions, and variations in the extent of preoperative pain. The use of a single-nerve catheter, instead of multiple catheters that included both the femoral and sciatic nerve, may have contributed to the failure of bupivacaine to produce superior results.⁶³

TREATMENT

Although numerous modalities exist for the treatment of neuropathic pain, many have shown only limited success (Table 24.1). Many of the studies of the effectiveness of pharmacotherapeutic agents have been done with small groups of patients and with no long-term follow-up.⁶⁴

Antidepressants, particularly those from the tricyclic group, and anticonvulsants are frequently administered for the treatment of neuropathic pain.^{8,43} However, double-blinded studies are needed to confirm their effectiveness in relieving phantom pain. Case reports show improvement in phantom limb pain using clonazepam⁶⁵ or fluoxetine, even in the absence of a coexisting affective disorder.⁶⁶ Beta-blockers have also

been used for phantom limb pain;^{8,67} their efficacy is unclear.³

Sherman⁶⁴ has found that burning and cramping components of phantom limb pain may each respond to different agents. Burning pain may be decreased by increasing the blood flow to the stump via nitroglycerine ointment or nifedipine, while muscle relaxants may relieve cramping pain.⁶⁴

Infusions of drugs may also decrease phantom limb pain. MacFarlane *et al.*⁷ found that five daily doses of IV lidocaine (3 mg/kg) given over 30 min for up to 4 days may produce prolonged relief. The oral antiarrhythmic agent, mexilitine, can be initiated if pain returns following an IV lidocaine infusion.⁷ A 1 mg/kg bolus of IV lidocaine has been given to treat chronic phantom pain and severe phantom pain flare-ups.³³

After several case reports revealed decreased phantom limb pain with calcitonin infusions, Jaeger and Maier⁶⁸ conducted a double-blind study with 200 IU of salmon calcitonin administered IV to patients with phantom pain. A second infusion was given to several patients who continued to experience pain. At 1-year follow-up 62% of amputees receiving calcitonin had greater than 75% pain relief. Relief extended to 2 years in 58% of the patients.⁶⁸

A great deal of excitement has been generated regarding the use of NMDA receptor antagonists in the treatment of neuropathic pain. The blockade of the NMDA receptor may reduce central hyperexcitability. In a randomized, double-blinded study of patients with persistent phantom limb pain, the NMDA receptor antagonist, IV ketamine, was given via a 0.1 mg/kg bolus over 5 min followed by an infusion of 7 µg/kg/min of ketamine for up to 45 min. During the infusion, and in some cases up to 3 days thereafter, ketamine relieved pain in the stump and the phantom limb to the same extent.³⁹ In a case report, ketamine produced pain relief when infused at 0.12 mg/kg/h in a

Table 24.1 Reported treatments used for phantom limb and stump pain

Medical interventions	Psychological interventions	Physical modalities	Invasive modalities
Opioids, antidepressants, anticonvulsants, sodium channel blockers, NMDA receptor antagonists, calcitonin	Relaxation, imagery, hypnosis, behavioral therapy, psychotherapy, biofeedback	Acupuncture, stump desensitizing, TENS to contralateral limb, auricular TENS, percussion of stump, prosthesis adjustment, heat or cold to stump, stump massage, stump ultrasound, physical therapy	Revisions of the stump, neuroma resection, sympathectomy, dorsal rhizotomy, dorsal root entry zone lesioning, dorsal cordotomy, anterolateral cordotomy, spinal cord stimulation, thalamic stimulation, stump neuroma injections, sympathetic blockade, intrathecal infusions, epidural infusions

pediatric amputee who developed severe phantom pain following chemotherapy.²⁷

Long-term opioid therapy can be used in the treatment of phantom limb pain; however, neuropathic pain may be less responsive to opioids than nociceptive pain and requires higher doses.⁶⁹ This may be in part attributed to a reduction in the number of opioid receptors expressed on c-fiber afferents following peripheral nerve damage.⁷⁰ The total amount of opioid required to achieve analgesia may be less when it is combined with other agents, such as the tricyclic antidepressants or anticonvulsants, that are used in pain modulation.

While ketamine has been shown to play a role in reducing neuropathic pain, its use may be limited by central nervous system side-effects such as insobriety.³⁹ Recently, a noncompetitive NMDA receptor antagonist, amantadine, was found to reduce surgical neuropathic pain in cancer patients.⁷¹ In a placebo-controlled randomized study, 200 mg of amantadine was infused over 3 h. Fifteen patients participated in this study. The types of neuropathic pain they had were associated with post-thoracotomy pain syndrome, post-mastectomy pain syndrome, ilioinguinal neuropathy, femoral neuropathy, and scar neuroma. Pain decreased by 85% following the infusion and continued for up to 48 h.⁷¹ The ability of IV amantadine to control phantom limb pain and the role of oral amantadine are unknown, and should be subjected to further evaluation.

Novel treatments that may have an impact on reducing phantom limb pain include cyclo-oxygenase inhibitors,⁷² nitric oxide synthesis inhibitors,⁷³ and axoplasmic transport modifiers.⁷⁴ Drugs that would prevent central sensitization are also being investigated.⁷⁵

Since no single form of treatment has been shown to consistently reduce phantom limb pain, an interdisciplinary approach may yield the best outcome. Physical therapy can help improve strength, flexibility, and balance in amputees. Refitting the prosthesis may result in a decrease in stump and phantom pain, although the severity of phantom pain does not appear to correlate with the amount of prosthesis use.¹⁹ Applying transcutaneous electrical nerve stimulation (TENS) to the contralateral limb may decrease phantom limb pain; however, exacerbation of pain has been documented from TENS use on the stump and should be avoided.^{4,76,77}

Katz and Melzack⁷⁷ reported painful throbbing and pressure of phantom limbs are reduced by low-frequency (4 Hz), high-intensity (10–30 V) auricular TENS.⁷⁷ The mechanism proposed for pain reduction is secondary to activation of brainstem structures that exert an inhibitory control over nociceptive neurons in

the spinal cord dorsal horn.⁸ Long-term follow-up was not done.

Other forms of therapy that have been described include acupuncture, guided imagery, hypnosis, and relaxation techniques.^{43,78} Sherman⁶⁴ found that patients with the burning component of phantom pain may experience a reduction in pain by temperature biofeedback or multiple sympathetic blockade, while cramping phantom pain may be decreased by biofeedback.

Intrathecal injections, with such agents as fentanyl, have been investigated for use in relieving phantom limb pain.⁷⁹ The partial opioid antagonist, buprenorphine, given intrathecally, has been shown to decrease baseline pain in several patients. This decrease is prolonged by switching to buprenorphine suppositories.⁸⁰ The selective neuronal voltage-sensitive calcium channel blocker, SNX-11, acts by blocking neurotransmitter release at the primary afferent nerve terminals. Continuous intrathecal administration of this drug reduced intractable phantom limb pain.⁸¹

Phantom limb pain generally does not respond to surgical intervention.³ Stump neuromas develop at the site of the severed end of peripheral nerves and may trigger phantom pain.⁴⁰ Surgical management may involve implanting the proximal end of the cut nerve into an adjacent bone or a nearby site.⁷ While this may decrease stump pain, it usually does not permanently relieve phantom pain.⁴ Neuroablative neurosurgical procedures are now rarely performed.

Anterolateral cordotomy provides only short-term relief, since the spinal cord contains a network of interconnecting fibers that will eventually resume the functions originally performed by the severed tract.⁸² Dorsal root entry zone (DREZ) lesioning can selectively abolish phantom limb, but not stump, pain.⁸² Saris *et al.*⁸² reported that 36% of such patients had pain relief with a follow-up period ranging from 6 months to 4 years. They also found that nine out of 22 patients developed minor but chronic neurologic deficits.⁸² The results of DREZ lesioning are more promising in patients who undergo traumatic amputation than in oncology patients.⁸³

Spinal cord stimulation has also been used for phantom limb pain.⁸⁴ Seigfried *et al.*⁸⁵ reported that 51% of patients with implanted spinal cord stimulators had a 50% or more decrease in pain, while 18% obtained a 25–50% reduction in pain. Long-term follow-up is needed to determine whether the initial relief is sustained over time.

Finally, intracranial neurostimulation has been used for phantom limb pain. Stimulation of the parvocellular part of the nucleus ventralis posterolateralis of the thalamus has led to a decrease in phantom limb pain;⁸⁶

however, in most cases pain control has not been permanent.³

CONCLUSION

An interdisciplinary approach to pain management and rehabilitation can provide amputees with the best chance of a pain-free outcome.⁸ Members of the team may include representatives from medical and surgical oncology, rehabilitation medicine, pain medicine, behavioral medicine, and nursing. Preoperative patient education programs are also essential.⁸⁷ Psychological support and reassurance can alleviate anxiety that often follows amputation. Amputees need to be aware of their

postoperative pain management options and to understand that their pain will be aggressively managed. It is important that these options also be addressed in the preoperative conference. Rehabilitation is initiated prior to the patient's discharge. In many amputees pain is the major limiting factor in rehabilitation. To achieve a functional lifestyle as soon as possible, it is mandatory that we use every available means to control pain.⁴⁰

If persistent pain develops, a comprehensive evaluation is necessary. The impact of the pain on the patient's psychosocial and physical functioning is an integral part of this assessment. A treatment plan based on the contributions of different specialists of the interdisciplinary team can then be formulated.

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Section 4

Limb-sparing Surgery

Review of Endoprosthetic Reconstruction in Limb-sparing Surgery

Robert Henshaw and Martin Malawer

OVERVIEW

Endoprosthetic replacement of segmental skeletal defects is the preferred technique of reconstruction after resection of bone sarcomas. Today, all of the major anatomic joints with their adjacent segmental bone can be reconstructed safely and reliably with a modular endoprosthetic replacement. Prosthetic reconstruction is routinely performed for the proximal femur, distal femur, total femur, proximal tibia, proximal humerus, and scapula. Allografts are rarely used.

A major advantage of a modular endoprosthetic system is intraoperative flexibility; it enables the surgeon to reconstruct defects of any size with minimal preoperative planning. Instead of performing a resection to match a prosthesis customized on the basis of imaging studies that are 4–8 weeks old, the surgeon can concentrate on performing the best possible resection indicated for the patient at the time of surgery. Overall survival analysis of large segmental replacements is approximately 90% at 10 years (reported at 98% for the proximal humerus and 90% for the distal femur).

This chapter reviews the indications and techniques for performing endoprosthetic replacements for bone tumors. Many of the described surgical techniques were developed by the senior author, placing emphasis on techniques for reconstructing the soft tissues after implantation of a modular endoprosthesis to optimize the functional outcome.

INTRODUCTION

The concept of limb-sparing surgery, or limb salvage, has gradually evolved over the past 25 years. Prior to this, the basic principles of surgical oncology for the extremities consisted solely of determining the correct level at which to perform an amputation. With the introduction of effective Adriamycin- and methotrexate-based chemotherapy protocols in the early 1970s at centers such as Memorial–Sloan Kettering, New York University, and the Children's Hospital of Philadelphia, surgeons such as Ralph Marcove, Kenneth Francis, and Hugh Watts developed techniques of limb-sparing surgery. Today, 90–95% of patients with extremity sarcomas who are treated at major centers specializing in musculoskeletal oncology can undergo successful limb-sparing procedures.

This dramatic alteration in patient care is the result of significant advances along many fronts, including:

1. improved understanding of tumor biology;
2. effective induction chemotherapy;
3. technical advances in surgical techniques;
4. better characterization of the biomechanics of the human skeleton;
5. advanced material engineering and manufacturing techniques;
6. the development of a reliable, stable modular prosthesis for reconstruction of the hip, shoulder, and knee.

This book focuses primarily on techniques of oncologic resection that have been developed by the authors over the past 20 years. Emphasis is placed on several principles that are key to the success of this technique. The first is identification and preservation of key neurologic and vascular structures in the limbs and pelvis. Second, the importance of achieving an appropriate oncologic margin cannot be overstated, for preservation of the limb should rarely, if ever, take precedence over the survival of the patient. Achieving safe margins requires meticulous surgical technique. Resection, however, is only the first stage of a limb-sparing procedure. Reconstruction of the axial skeleton and restoration of soft-tissue coverage for optimal function are also performed.

The purpose of Chapter 25 is to review the major medical and surgical considerations in selecting a patient for limb salvage and to discuss the options available for reconstructing the defect remaining after an oncologic resection. An overview of the surgical techniques for reconstruction of each major joint, as developed and currently practiced by the authors, is presented.

PATIENT SELECTION

Appropriate patient selection for limb-sparing procedures is essential to ensure good, consistent results. Although the introduction of chemotherapy for osteosarcoma was a major impetus for the development of techniques for limb-sparing surgery, increasingly high long-term survival rates have placed greater emphasis on the functional outcome and longevity of the reconstruction. Today's patient expects a solution that addresses his or her functional, cosmetic, and psychological needs.

The location and involvement of critical anatomic structures are often the determining factors in selecting patients for limb salvage versus a primary amputation. With the use of modern neoadjuvant (i.e. preoperative, induction) chemotherapy, many patients who are initially not suited for a limb-sparing procedure may ultimately become candidates for such surgery. Therefore, the final surgical decision is often not made until a patient has been re-evaluated following the completion of neoadjuvant treatment. Improvements in chemotherapy have increased the pool of patients amenable to limb-sparing procedures.

Limb-sparing procedures, moreover, are not necessarily limited to patients who respond to treatment. Patients with very poor prognostic factors, such as those with metastatic disease upon initial presentation and those who fail to respond to chemotherapy, often require significant palliative surgery in order to maintain an acceptable quality of life. Because these individuals have a limited life expectancy, amputation should be avoided in all but the extreme cases who require emergency palliation. Radical or mutilating procedures are not appropriate for patients if there is no hope of prolonging their survival. The surgical intervention selected is dependent on where a given patient falls within the spectrum of potential oncologic outcomes.

ROLE OF IMAGING STUDIES AND PATIENT STAGING

Advanced imaging modalities have vastly improved our ability to accurately determine the extent of tumor prior to surgical exploration. High-resolution axial and multiplanar images from computed tomography (CT) or magnetic resonance imaging (MRI) scans can determine the extent of the tumor and its relationship to the surrounding anatomic compartments. CT imaging of the chest is performed to detect pulmonary metastases, and technetium bone scanning of the entire skeleton is performed to detect the presence of metastatic disease. For bone sarcomas and most soft-

tissue sarcomas, the lungs and skeleton account for the vast majority of all sites for metastases. High-quality imaging studies, combined with detailed histologic grading of a biopsy (preferably done by a core needle), allows for accurate staging.

Early attempts to stratify patients on the basis of tumor size failed to account for the biologic behavior of a given tumor. A more reliable approach is a staging scheme that accommodates the fact that the aggressive nature of a tumor can be graded by the histologic appearance of the cells and their nuclei. William Enneking¹ added to this the concept of an anatomic compartment, which acts as a relative barrier to tumor spread. His staging system combined tumor grade and anatomic extent in a simple, yet easily reproducible and prognostically significant format. The Musculoskeletal Tumor Society has adopted this system as its preferred method for staging extremity sarcomas.

Limb salvage for Stage I (low-grade) and Stage IIA (high-grade, intracompartmental) lesions is now routinely performed, because these tumors are easily resectable. A majority of the surrounding soft tissue can routinely be preserved. For these patients, reconstruction is typically limited to restoration of skeletal stability. Stage IIB tumors, which can involve multiple compartments, may be unresectable at presentation. Neoadjuvant chemotherapy can have a dramatic role in converting patients with tumors that are initially thought to be unresectable into candidates for limb-sparing surgery. Such a conversion may occur when chemotherapy causes the tumor to shrink, thereby freeing critical neurovascular structures. Finally, patients with Stage III disease may be considered for palliative resections in lieu of amputation, provided that prolonged immobilization or delayed wound healing does not interfere with their medical treatment. In patients with Stage IIB and III tumors, skeletal and soft-tissue reconstruction must be performed.

STAGES OF LIMB-SPARING SURGERY

A successful limb-sparing procedure can be divided into three stages, each of which directly affects patient outcome and survival. First and foremost, tumor resection must spare significant structures. Second, a stable, painless skeletal reconstruction must be accomplished. Third, the surrounding and supporting soft tissue is required to restore function and skeletal reconstruction.

As the techniques of surgical resection have been refined, the number of patients that fulfill these categories has increased. For example, involvement of a major vascular bundle formerly mandated an amputation. Today, major vessels are routinely resected

en-bloc with the tumor; this is followed by vascular reconstruction utilizing an artificial graft or reversed vein graft. Likewise, use of local rotational pedicle flaps or microvascular free flaps allows for reconstruction of patients whose tumor resection necessitated removal of significant portions of the surrounding soft tissue. Such flaps provide the muscle and skin coverage necessary to restore limb function and prevent postoperative periprosthetic infections.

RECONSTRUCTIVE OPTIONS FOR SKELETAL DEFECTS

There are four major methods of reconstructing a skeletal defect. These are as follows:

1. *Resection arthrodesis.* Prior to the routine use of chemotherapy in the 1970s, resection of a sarcoma entailed the loss of significant amounts of muscle. Little tissue was left for functional reconstruction. In these early days of limb salvage, resection arthrodesis was the main method of reconstruction (Figure 25.1). Its primary advantages were to restore skeletal stability and produce a long-term, durable reconstruction. No attempt was made to restore motion at the resected joint, however, and many patients expressed dissatisfaction with their loss of function. Today, effective chemotherapy allows for the preservation of significant functional muscle groups, and the use of rotational flaps can restore function when muscle is lost. As a result, resection arthrodesis is rarely recommended as the primary method of reconstruction today; in fact, a number of long-term survivors originally treated with arthrodeses around the knee have undergone conversion to endoprosthetic reconstruction to restore their ability to passively flex and extend the knee.
2. *Osteoarticular or massive allografts.* Allograft reconstruction was championed in the 1970s as a biologic solution to the problem of restoring a segmental defect of the skeleton. Despite technical improvements in the method of fixation, and in the processing of the allograft to preserve cartilage cells and reduce contaminants, this method of reconstruction has significant complications. These include early complications, such as infection, nonunion and joint instability, and late complications such as instability and allograft fracture. Overall complication rates can exceed 50%, including an infection rate of 30%, even when performed at a major center.² As a result, allograft procedures are preferred at only a few centers today. Many surgeons avoid them entirely in patients undergoing chemotherapy for high-grade sarcomas.

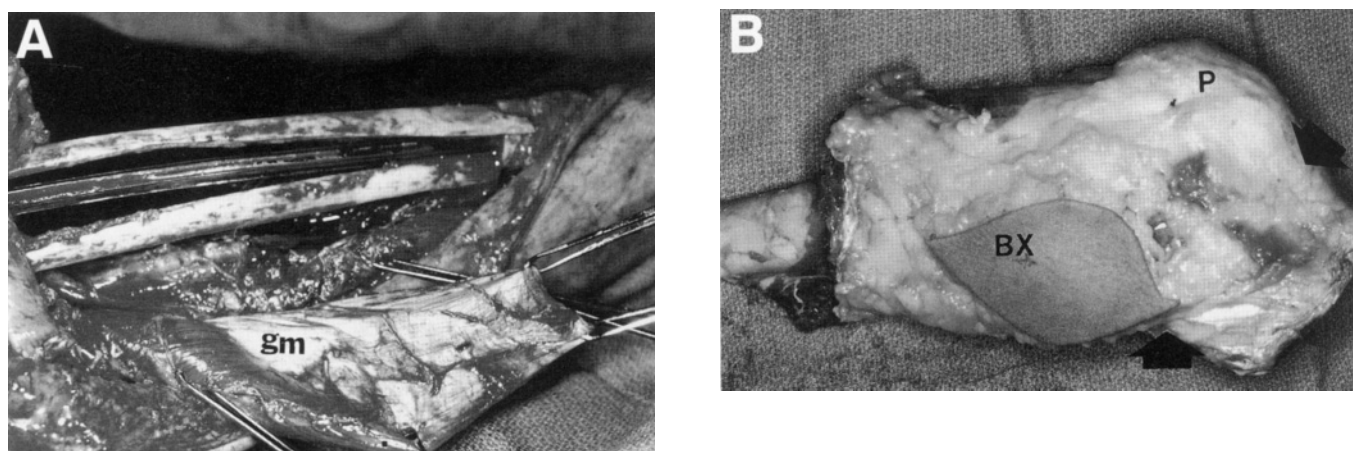


Figure 25.1 Resection arthrodesis (per Enneking). (A) Intraoperative photograph demonstrating the dual fibular reconstruction with an intramedullary rod fixation following resection of the distal femur. This technique of reconstruction was popularized during the 1970s by Dr William F. Enneking prior to the development of reliable reconstruction prostheses. Note the medial gastrocnemius flap (gm) has been mobilized for rotation closure of the defect. (B) Gross specimen following an extra-articular resection of the distal femur (P = patella). Note the biopsy tract (BX) was removed with the specimen. The arrows indicate the level of the joint. This was the standard technique for resection during the 1970s and early 1980s. Today this technique is rarely performed.

Currently, we perform allograft reconstruction for the rare patient with a diaphyseal lesion that can be reconstructed with an intercalary allograft or for very young patients who might be expected to develop substantial leg-length discrepancies as they grow. For the latter patients an allograft can preserve additional growth plates and reduce the expected leg-length discrepancy. Ultimately, such patients often require conversion to an endoprosthesis because their functional demands result in fracture of the allograft.

3. **Endoprosthesis.** Endoprosthetic reconstruction is a highly successful and durable method for the restoration of skeletal integrity and joint function. Use of a cemented stem provides immediate fixation, which allows for early mobilization and rehabilitation. Extensive experience in joint replacement has led to the development of materials suited for long-term prosthetic survival; at the same time, advances in the use of local rotational flaps have improved joint stability and simultaneously reduced the risk of infection. Since the mid-1980s custom-manufactured endoprostheses have been replaced by modular systems with standard instrumentation that vastly expands the reconstruction options (Figure 25.2). This is the authors' preferred method of reconstruction and this chapter will expand on the topic, below.
4. **Allograft-prosthetic composite (APC).** APCs can be viewed as a transitional step between allografts and endoprostheses. This procedure became popular

when surgeons began to abandon pure osteo-articular allografts. APCs were thought to provide the benefits of a biologic reconstruction along with the immediate stability achieved by a cemented endoprosthesis. Experience has shown that this method has the same high rate of early complications (i.e. infection and nonunion) as does standard allograft reconstruction. Accordingly, this method is better suited for a patient undergoing revision of a failed allograft, rather than a patient undergoing chemotherapy for a sarcoma.³

HISTORY OF ENDOPROSTHETIC RECONSTRUCTION

The earliest published example of an endoprosthetic reconstruction following treatment of a bone tumor dates to 1940, when Austin Moore and Harold Bohlman implanted a vitallium proximal femur in a patient with a giant-cell tumor. In the early 1970s Kenneth Francis and Ralph Marcove ushered in the current age of endoprosthetic reconstruction following radical resection of osteosarcomas by developing a distal femoral and a total femoral replacement, respectively (Figure 25.3).⁴

This new concept of limb-sparing surgery for sarcoma patients was based on the hope that Adriamycin and methotrexate, newly introduced for osteosarcoma in the early 1970s, would permit a safe limb-sparing resection in lieu of primary amputation. However, it was soon recognized that the 6–8 week lag time between diagnosis and the creation of a custom

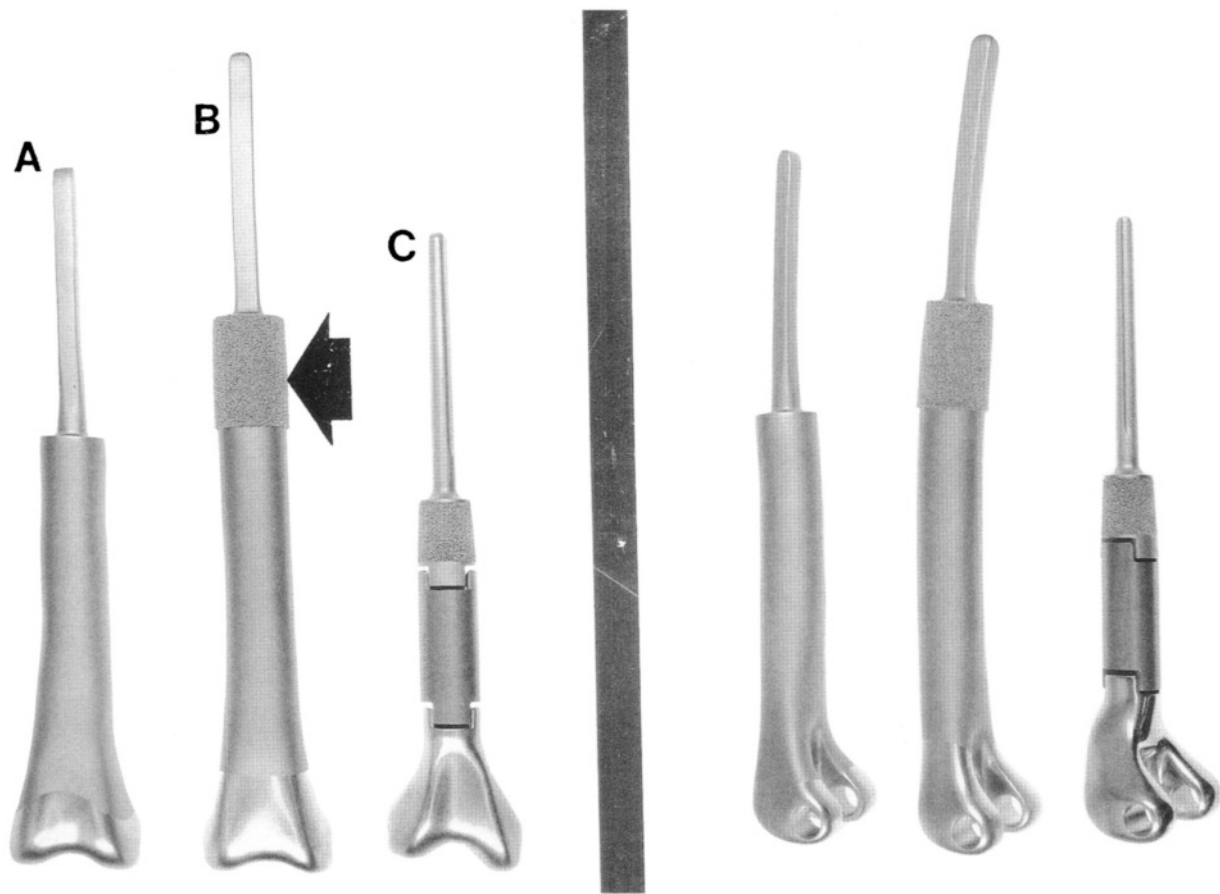


Figure 25.2 Types of distal femoral replacements. (A) Anterior–posterior view. (B) Lateral view. A = initial custom prosthesis used between 1981 and 1985; B = similar prosthesis with porous coating adjacent to the stem (arrow) to permit intracortical bone fixation: this prosthesis was first used in 1985; C = Modular prosthesis (Howmedica, Inc., Allendale, NJ) initially used in 1988 (see text). The modular design is presently used for most anatomic sites.

endoprosthesis for a given patient could have a negative impact on survival. As a result, Gerry Rosen and Ralph Marcove invented the concept of induction (i.e. pre-operative or neoadjuvant) chemotherapy, according to which patients with osteosarcomas received chemotherapy during the interval from time of diagnosis of the tumor to the delivery of that patient's custom implant.⁴ Induction chemotherapy is now administered to patients with a wide variety of cancers.

Specific examples of endoprosthetic reconstructions, that will be discussed in detail in this chapter, include the following:

Hip (Proximal Femur, Saddle)

Tumors involving the proximal femur, which include both primary sarcomas and metastatic carcinomas, are extremely common. Following resection of a primary tumor or fracture through a subtrochanteric metastatic lesion, the proximal femur can be readily replaced. Typically, a bipolar hemiarthroplasty is used for the hip

joint with reconstruction of the hip capsule to prevent complications related to postoperative dislocation. Hip abductors can be reconstructed by attaching them directly to the prosthesis via a laterally placed metal loop. Much less common are resections of the entire hip joint (type II pelvic resection and its modifications). This defect can be reconstructed with a saddle prosthesis, a device that derives its name from the U-shaped component that articulates with the remaining iliac wing. Stability is achieved by balancing the muscle tension between the medial iliopsoas and the lateral hip abductors.

Knee (Distal Femur) (Figure 25.4)

The distal femur is the most common site for primary bone sarcomas. Prosthetic reconstruction requires a unique combination of flexibility and stability, because the knee capsule and the cruciate and collateral ligaments are removed during the resection. The rotating hinge design permits both flexion and extension, as

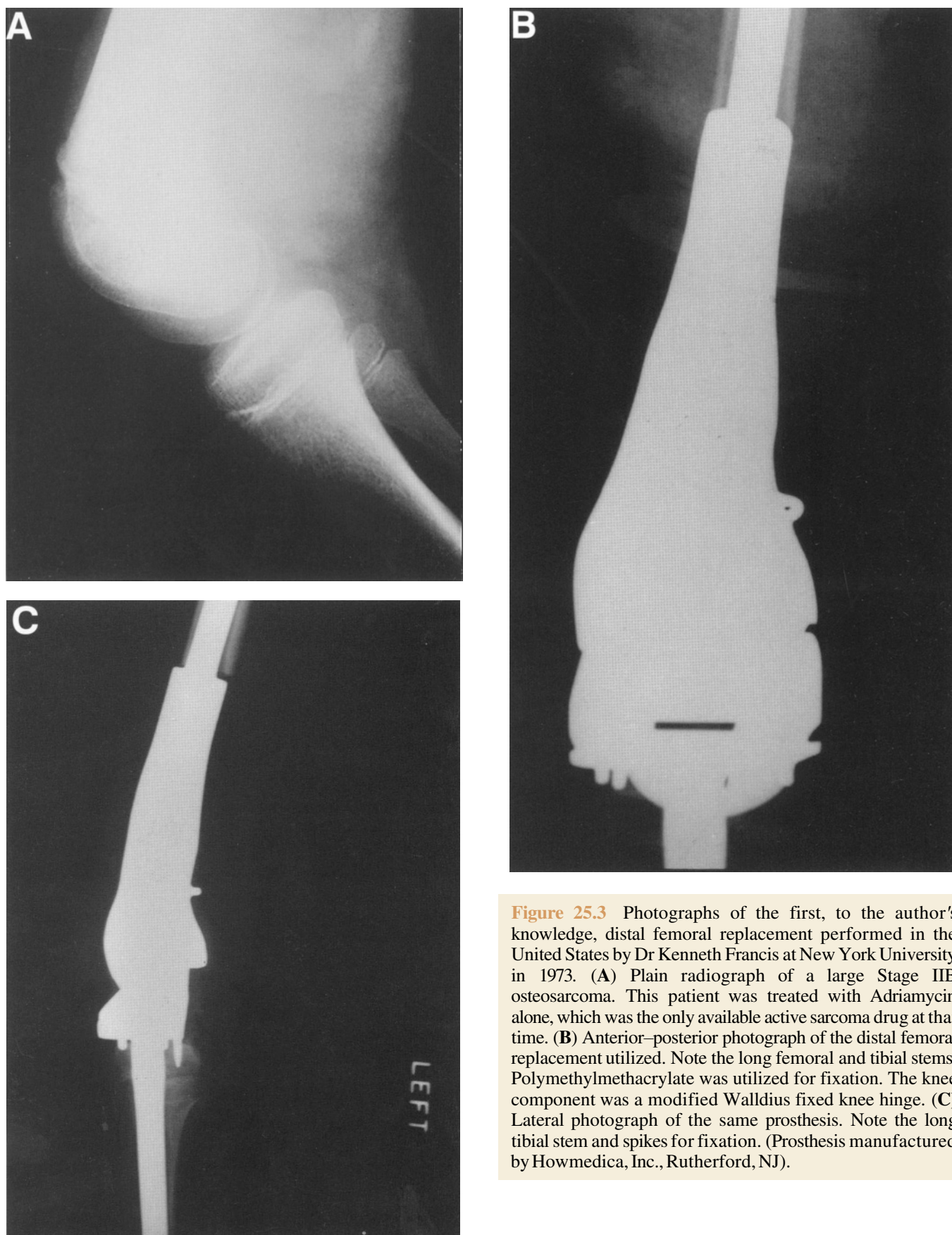


Figure 25.3 Photographs of the first, to the author's knowledge, distal femoral replacement performed in the United States by Dr Kenneth Francis at New York University in 1973. (A) Plain radiograph of a large Stage IIB osteosarcoma. This patient was treated with Adriamycin alone, which was the only available active sarcoma drug at that time. (B) Anterior–posterior photograph of the distal femoral replacement utilized. Note the long femoral and tibial stems. Polymethylmethacrylate was utilized for fixation. The knee component was a modified Walldius fixed knee hinge. (C) Lateral photograph of the same prosthesis. Note the long tibial stem and spikes for fixation. (Prosthesis manufactured by Howmedica, Inc., Rutherford, NJ).

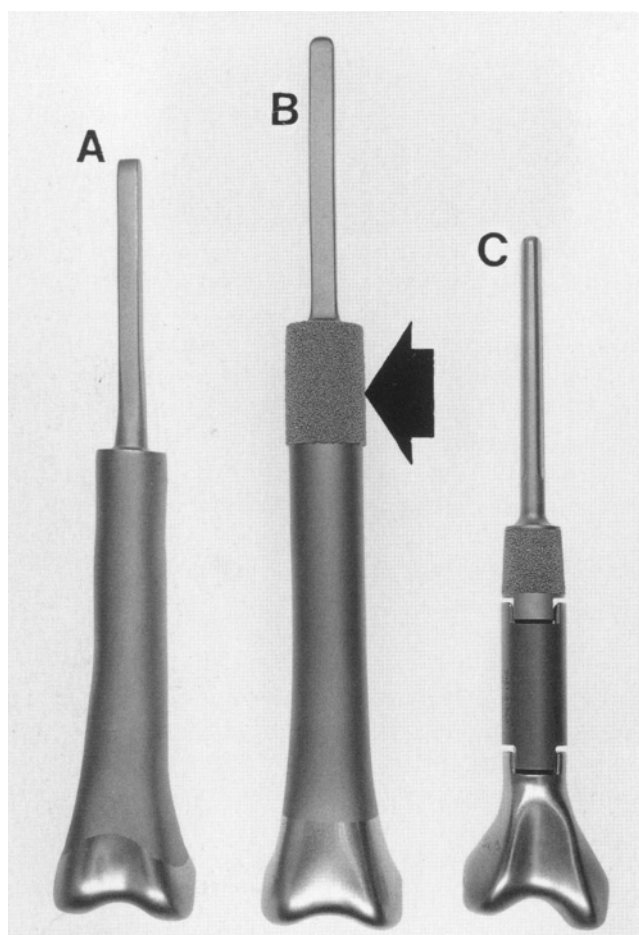


Figure 25.4 Custom distal femoral prostheses used between 1982 and 2000. (Knee component not shown) (A) Original custom prosthesis (1982). (B) Custom prosthesis (1984–1988) with porous collar (solid arrow) to permit extracortical bone fixation and soft-tissue attachments (1984–1988). (C) Modular segmental prosthesis. This was the original segmental design (1988) which is currently in use today with some modifications (Courtesy Howmedica, Inc., Rutherford, NJ).

well as rotation through the knee, while maintaining stability in varus/valgus and anterior/posterior planes. Reconstruction of the extensor mechanism is rarely required since the patella can usually be saved during the resection.

Total Femur

Patients presenting with the rare sarcoma that has an extensive intramedullary extent, as well as patients with multiple failed total joints and little remaining bone stock, can be treated with a total femoral replacement. A natural combination of the distal

femoral rotating hinge and the proximal femoral replacement with a bipolar head, this type of reconstruction has proven to be extremely durable as a result of the degrees of freedom that are afforded by the two separate, but related, joints.

Proximal Tibia

The tibia is unique given its subcutaneous border along the anterior leg. Any form of reconstruction can be jeopardized by even minimal amounts of skin necrosis. Routine use of a gastrocnemius rotation flap has dramatically reduced the incidence of postoperative complications. Joint stability at the knee is assured by using the same rotating hinge design used for distal femoral replacements.

Shoulder (Proximal Humerus)

High-grade sarcomas of the proximal humerus require extra-articular resection, that includes the entire rotator cuff and deltoid muscles. The functional outcome of a proximal humeral replacement following this type of resection is therefore greatly restricted by lack of functional muscle. A combination of static and dynamic suspension, including transfer of the pectoralis muscle, stabilizes the proximal humerus to the scapula, and permits painless and functional use of the elbow, wrist, and hand.

Scapula (Scapulohumeral)

Following total resection of the scapula, a scapular prosthesis helps lateralize the humerus and stabilize the shoulder joint. Resurfacing the humeral head and reconstruction of the capsule with a Dacron graft is necessary for optimal stability. Functional outcome depends on the amount of muscle preserved during resection.

Elbow

The elbow joint is rarely involved by sarcomas or metastatic disease. Customized, hinged implants with small-caliber stems to fit the ulna and distal humeral canals may be used, provided that sufficient soft tissue remains to cover the prosthesis.

Total Humerus

This implant is a combination of a proximal humeral implant and an elbow replacement. The indications for this procedure are rare, but a sensate, functional hand remains preferable to an amputation.

Calcaneus

There has been one reported case of a total calcaneal prosthesis implanted in lieu of a below-knee amputation in a patient with osteosarcoma. Five years after surgery this patient is fully ambulatory and does not depend on assistive devices.

Expandable Implants for the Skeletally Immature Patient

Reconstruction of the axial skeleton in immature patients is problematic. Children over the age of 10–12 years can often be treated as adults, using smaller versions of the modular prostheses, occasionally in combination with contralateral epiphyseodesis to equalize leg length at skeletal maturity. Below the age of 6, primary amputation remains the preferred method of tumor resection, given the extraordinary difficulty in obtaining a proper oncologic margin around the critical neurovascular bundles. In children between the ages of 6 and 10–12 reconstruction is feasible, but limb-length inequality becomes functionally disabling as the child grows. Implants that can be expanded multiple times during growth permit prosthetic reconstruction for these children. These custom-created implants have been used both in the upper and lower extremities with mixed results. Mechanical failures of the expansion mechanism are not uncommon (see [Figure 25.10](#), arrows). Many patients must undergo as many as 10 operative procedures to ensure limb equalization during the period of active growth.

As experience with prosthetic design and implantation grew, a wide variety of custom implants became available ([Figure 25.2](#)). All of the early prostheses, however, were individually designed and manufactured on a one-off basis. Prosthetic failures related to design flaws and errors in manufacturing were common. Improved design concepts and manufacturing techniques developed during the production of standard total hip and total knee prostheses were eventually applied to these “mega” prostheses ([Figure 25.4](#)). However, design improvements requiring increasingly complex mechanical geometry, and the increasing use of difficult-to-process alloys such as titanium and cobalt chrome, have lengthened the manufacturing time. These considerations offset the gains associated with long experience in handling custom implants and the reduced time needed to design the actual implant. As a result the minimum time between design and delivery of a sterilized custom endoprosthesis remains 6–12 weeks.

Endoprosthetic reconstruction is associated both with mechanical failures (e.g. stem fracture, erosion and failure of polyethylene components) and nonmechanical

failures (e.g. infection and aseptic loosening). Advances in design and surgical techniques have reduced these problems substantially. However, the problem unique to custom endoprosthetic implants that cannot be controlled for is that the planned resection may need to be revised at the time of surgery. This is particularly true when the tumor grows significantly during the time that the prosthesis is being manufactured, or when there is a difference in the preoperative imaging measurements and the actual dimensions of the patient’s bony anatomy or size of the tumor. Attempts to use a component that is not the appropriate size can significantly jeopardize the oncologic result, the functional result, or both.

Flexibility at the time of surgical reconstruction can be increased by incorporating modular features into the prosthesis ([Figure 25.5](#)). Although modularity increases the complexity of the mechanical construct, and carries with it risk of failure associated with the sum of all of the components, it has several significant benefits. The primary advantage is flexibility: the surgeon can concentrate on performing the best-possible oncologic resection knowing that any changes in the preoperative plan can be accommodated by having at hand the components needed to reconstruct the actual skeletal defect. The use of standard components also allows the surgeon to articulate trial components during the procedure, and to repeatedly modify and test a reconstruction before selecting and assembling the final prosthesis. Standardization of components also permits the implant manufacturer to greatly increase the level of quality control while reducing the cost of manufacturing through economies of scale. Modular systems can also reduce the overall inventory needed to provide a large choice of prosthetic shapes and sizes. Finally, a modular system lends itself to reconstructive situations outside of oncologic resections immediately available as a backup option for selected patients, such as those undergoing difficult joint revision surgery.

The Howmedica Modular Replacement System (HMRS, Howmedica International) designed and manufactured in Europe, was a first-generation modular endoprosthetic system. It featured intramedullary, cementless, press-fit stems supported by external flanges and cortical transfixation screws. The knee mechanism consisted of a simple hinge design. Significant problems encountered with this device included aseptic stem loosening (osteolysis), substantial stress shielding with bone resorption, screw fracture and migration, and a greater than 40% polyethylene failure rate for the knee mechanism.⁵ As a result this system has rarely been used in the United States.

A second-generation limited modular system from Europe currently available in the United States is the

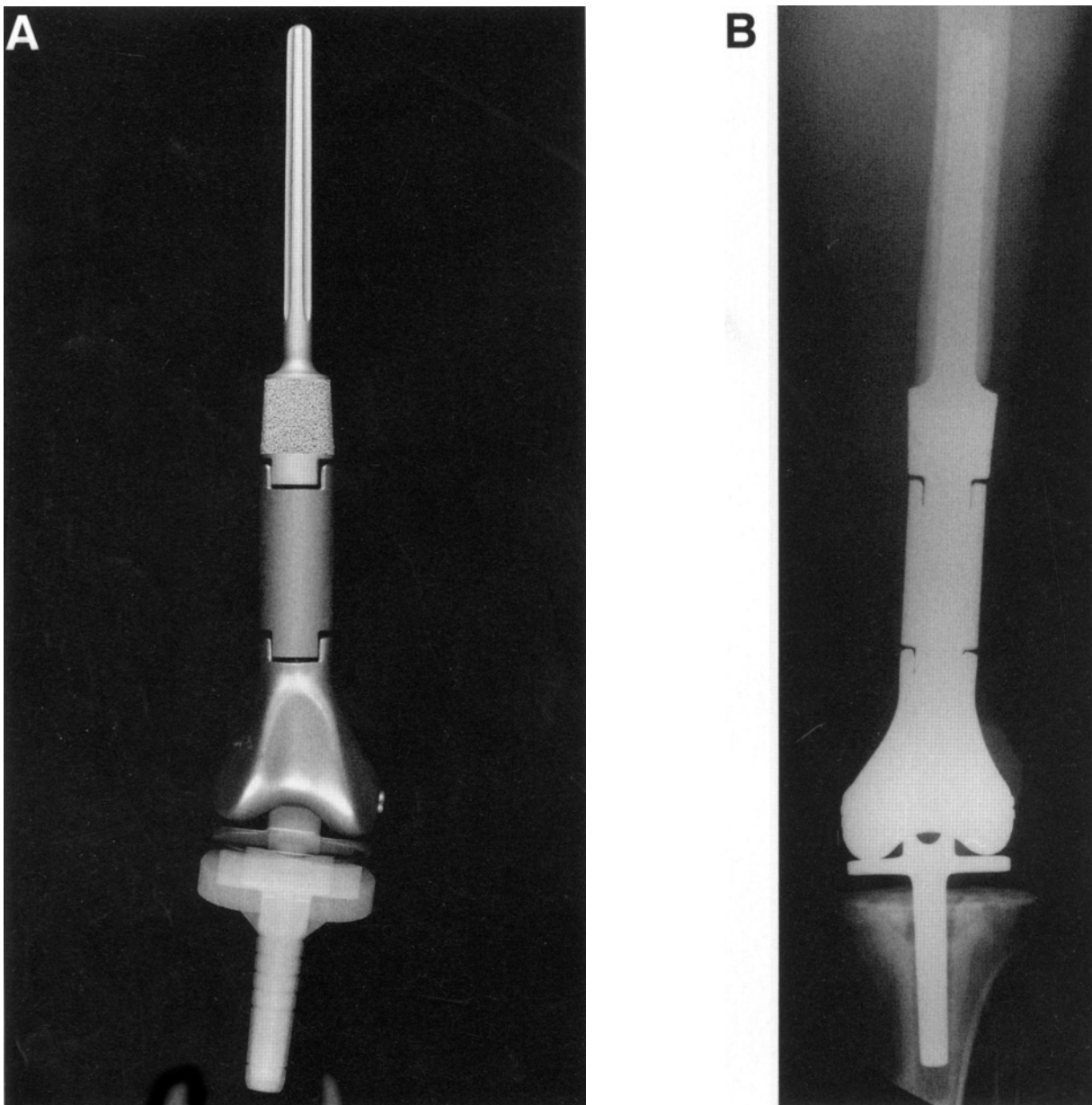


Figure 25.5 (see also following page) Modular replacement system (Howmedica, Inc.). (A) A distal femoral Modular Replacement System showing the stem, body, and condyles with the tibial insert (polyethylene) in which a tibial bearing plug (metal) is inserted. (B) Anterior-posterior photograph showing a distal femoral Modular Replacement System prosthesis in place. (C) Multi-phase photograph of the distal femur and proximal tibial component that demonstrates the range of flexion that is permitted with the Kinematic rotating hinge knee component. (D) Multi-phase photograph of the distal femoral modular replacement showing the rotation that is permitted within the tibial polyethylene component. Note, there is almost a complete freedom of rotation. In order to control this rotation, good muscle reconstruction is essential.

modular saddle endoprosthesis (Link America, Danville, New Jersey). This prosthesis, designed for the treatment of infected, failed total hip replacements, has been modified to allow for reconstruction of the hip following resection of the pelvis. The unique feature of

this system is the saddle, which is a U-shaped component that straddles the ilium, allowing motion in flexion/extension, and abduction/adduction by rocking in the AP and lateral planes against the bone. An additional ring containing polyethylene permits

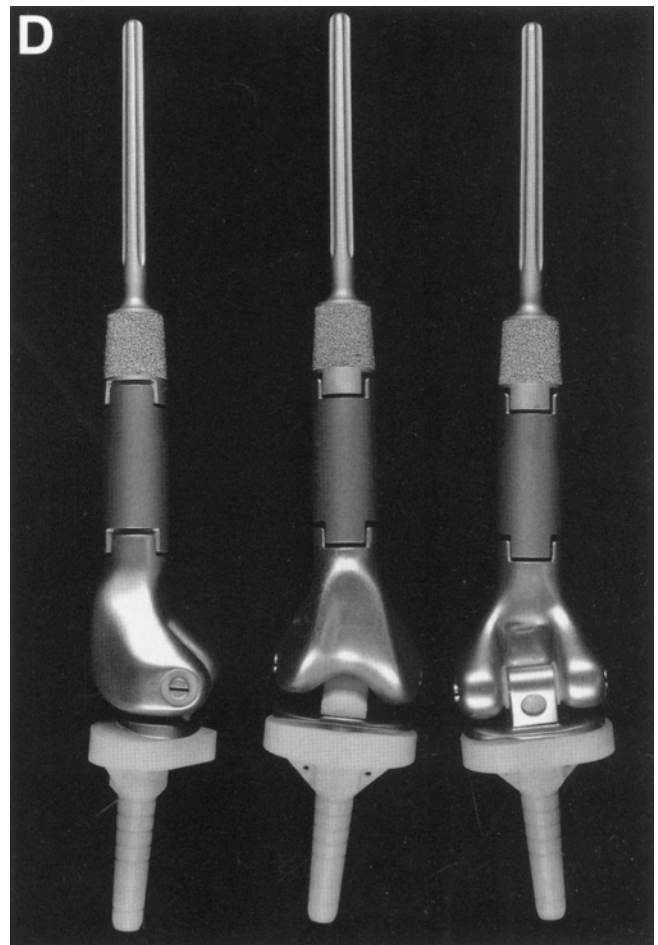
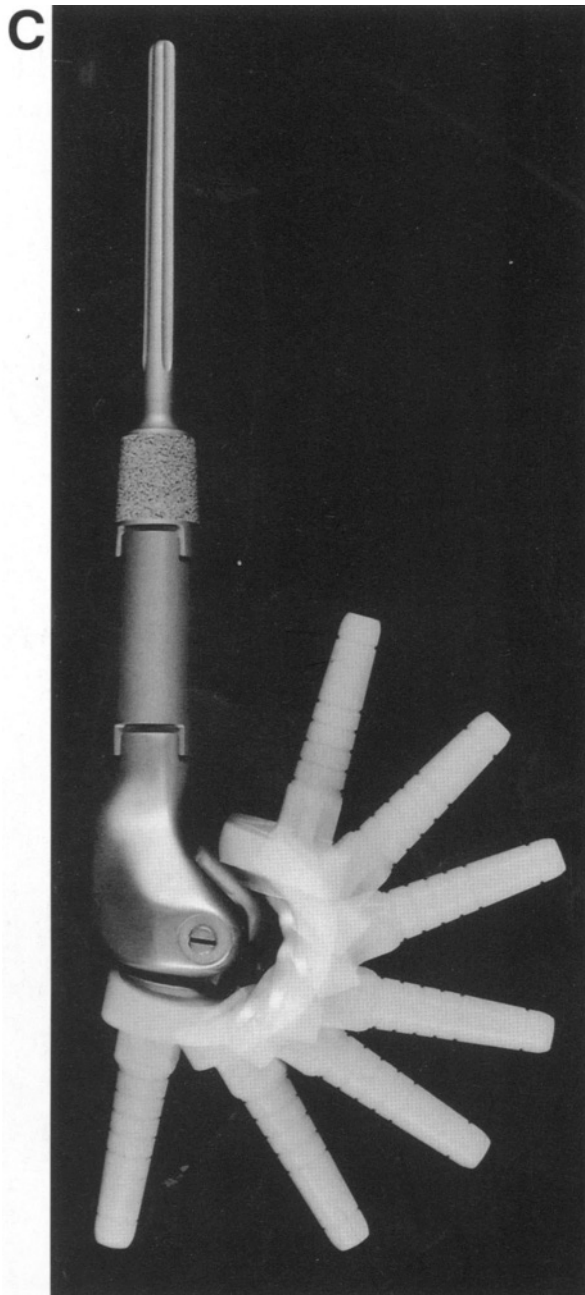


Figure 25.5 C, D

rotation, and increases the degree of freedom for the joint. The saddle component connects to a series of interchangeable modular bodies that, in turn, connect to a standard cemented hip component. This device preserves limb length following resection of the periacetabulum (type 2 pelvic resection, modified internal hemipelvectomy) while functioning like a total hip prosthesis. The clinical and functional results following saddle reconstruction of the pelvis with this system have been extremely good.⁶

CURRENT DESIGNS – THE MODULAR REPLACEMENT SYSTEM (MRS)

A second-generation universal system, originally called the modular segmental replacement system (MSRS) and recently renamed the modular replacement system (MRS), was introduced in 1988 (Howmedica Inc., Rutherford, NJ). This system was designed to provide modular replacements for the proximal humerus, proximal femur, total femur, distal femur, and proximal

tibia. Careful failure analysis of custom endoprostheses guided the design of the new modular system. Significant design features are the following:

1. *Cemented stems.* The use of bone cement (methyl methacrylate) has a substantial track record in joint replacement. Long-term outcome studies now cover nearly 25 years. Cement is well tolerated biologically and functions as a grout that compensates for any mismatch between the geometry of the medullary canal and the prosthetic stem. Additionally, aseptic loosening, which was once believed to be associated with the bone cement and even termed "cement disease", has now been attributed to the biologic response to wear debris, particularly polyethylene. Cemented stems ensure immediate fixation, avoid the need for postoperative bracing or prolonged non-weight-bearing, and permit early rehabilitation.
2. *Multiple stem diameters.* Experience with custom endoprostheses demonstrated a substantial risk of stem fracture secondary to fatigue failure when small-diameter stems were used. The modular system permits the use of the largest stem diameter possible for a given patient, thereby minimizing this risk. In addition, the use of a facing reamer that matches the outer radius of the stem/body junction allows for a perfect seat for the prosthesis, and protects the stem from bending stresses.
3. *Circumferential porous coating.* A porous surface composed of two layers of sintered beads around the body of the prosthesis was originally designed to permit the ingrowth of bone graft placed at the bone/prosthesis junction (extraskeletal fixation) (Figure 25.6). This bone graft can protect the prosthetic stem by sharing all bending and loading stresses on the implant. A potentially more significant benefit of this feature is that it supports the ingrowth of soft tissue, which produces a seal between the debris-laden articular and periprosthetic fluid and the vulnerable bone–cement–stem interface. Termed the "biologic noose", this seal has been shown by Ward *et al.*⁷ to essentially eliminate the risk of osteolysis when used in endoprosthetic reconstructions.⁸
4. *Rotating hinge knee* (Figure 25.5C). The Kinematic rotating hinge knee, originally designed as a semi-constrained total knee replacement, was adopted for this system because it not only provides stability but also offers a high degree of freedom of motion. This is critical for reconstructing the knee when all of the cruciates and collateral ligaments have been resected or are otherwise incompetent.

Other important new features of this system include full instrumentation to assist in preparing the canal for implantation, and a series of assembly modules that

hold and impact the modular components together. Metal loops and porous coated surfaces exist at the important insertion points of significant functional tendons (e.g. extensor mechanism for a proximal tibial replacement) to permit dependable soft-tissue reattachment and fibrous ingrowth into the prosthesis.

BIOMECHANICAL CONSIDERATIONS FOR ENDOPROSTHETIC RECONSTRUCTION

Prosthetic Design

Careful observation of modes of failure over time is critical to understanding the mechanical and material limitations of any manufactured device. Reports of long-term clinical experience with various custom endoprosthetic systems served as a basis for many of the design features of the current MRS. The process of observation and redesign should not, however, be viewed as a one-time activity. Continued analysis of the results of each modification to the system is required to ensure that corrections of existing problems do not in themselves lead to unforeseen new difficulties.

For the early devices a major mode of catastrophic mechanical failure was fracture of the intramedullary stem. This problem was caused by a number of unrelated factors. Errors in the mixture of the alloys used in the manufacturing process, as well as in processes used in creating the device (e.g. casting, forging, machining, tempering) can leave microscopic structural defects within the stem that can be susceptible to fatigue failure over time. The biomechanical loads carried by an endoprosthesis can be staggering. Experiments with instrumented hip replacements have documented a joint reaction force of 2.3–3.3 times body weight during routine weight-bearing and 0.86–2.19 times body weight during single-leg stance.⁸ Much greater loads occur with impact activities. An average person has a stride length of around 0.6 m when walking at a normal pace⁹ of 1.2 m/s. This translates to two steps (heel strike to heel strike) every second. If one assumes that an average of 15 min of every waking hour are spent walking, this equates to over 10 million cycles of loading each year. What is impressive is not that some stems fail over time but that many stems survive.

The most important determinant of the strength of a stem is its cross-sectional diameter. Resistance to bending in a given plane is proportional to the radius in that plane raised to the fourth power. Consequently, small increases in the diameter of the stem lead to significant gains in rigidity and resistance to bending. This is supported by the fact that the stems that typically fracture in custom implants are typically very small (≤ 9 mm in diameter).¹⁰ The MRS system enables

the surgeon to implant the largest-diameter stem that can fit within the intramedullary canal. This factor alone can dramatically reduce the risk of stem failure.

Modular systems, however, require a dependable method of assembly. The Morse taper, and its many proprietary modifications, enables the surgeon to assemble a prosthesis simply by the impacting of its components (Figure 25.6A). Long-term results of

modular hip replacements have made orthopedic surgeons familiar with this method of fixation. While isolated examples of component dissociation have been reported for various modular implants of all designs, our experience with over 100 MRS implants has failed to reveal any problems with this taper. A crucial step in the assembly is to ensure that the taper is completely dry and free of debris that may interfere with complete

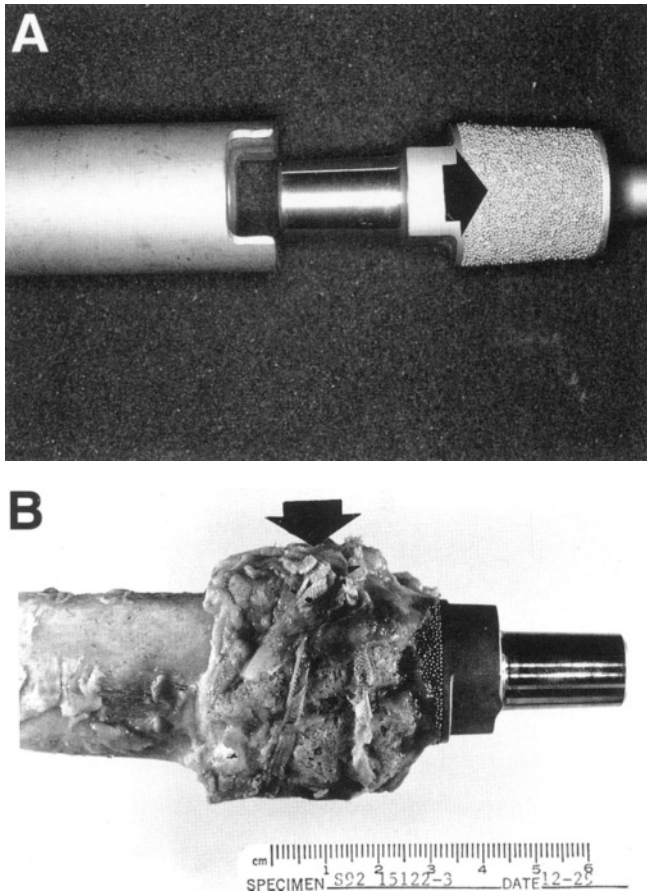


Figure 25.6 Extracortical fixation of a distal femoral prosthesis. (A) Close-up of the taper of the Modular Replacement System (Howmedica, Inc., Rutherford, NJ). Note the porous coating of the body of the stem (arrow). (B) Autopsy retrieval of distal femoral prosthesis. The bone graft (arrow) is well fixed to the porous coating. Note the beads are hardly visible. The Dacron (3 mm) tape is intact and is utilized to fix the autogenous bone graft to the porous-coated segment of the prosthesis. Note there is no evidence of corrosion of the taper. This prosthesis was in for 5 years. (C) Typical radiographic view of extracortical bone fixation (arrows) from the host bone to the porous-coated segment of a custom prosthesis. This is approximately 4 years since implantation. Extracortical bone fixation was first developed as a practical concept following the introduction of porous coating by Howmedica (Rutherford, NJ) during the early 1980s.

seating of the taper. Failure to do this can result in a loose fit. The ability to create a loose fit has actually been used to advantage clinically in patients requiring a temporary prosthesis (such as a spacer for treating an infection) that can be easily disassembled to permit revision surgery.

A second method of protecting a stem from failure takes advantage of the biologic properties of bone. A bone bridge, termed "extracortical bone fixation", is created between the outer diameter of the prosthetic body and the outer bone cortex, bypassing the relatively vulnerable transition zone between the prosthetic body, prosthetic stem, cement, and diaphyseal bone (Figure 25.6).¹¹ The bone bridge protects the stem by increasing the diameter of the composite mechanical structure that resists bending moment, thereby reducing the overall stress applied to the actual stem. This method of biologic fixation, however, requires that the bone graft adheres or attaches to the prosthesis. Early attempts at simple onlay bone graft were disappointing because the graft was often resorbed. Fixation of the onlay graft with a circumferential Dacron tape, however, has been shown to provide enough compression so that the bone graft not only adheres to but also hypertrophies around the prosthesis. This outcome was the original impetus for placing porous-coated surfaces on the prosthetic body adjacent to the stem. Clinical experience has shown that this effect is readily reproducible. Additional application of demineralized bone matrix containing bone morphogenic protein (BMP) is a promising method of further improving this method of fixation.

A nonbiologic method of protecting the stem is an external flange, which is utilized in the European modular system. Biomechanically, the flange increases the diameter of the composite mechanical structure. Unfortunately, the clinical results of flanges have been disappointing. Significant stress shielding and resulting bone loss of the cortex located between the stem and the external flange occur. This destabilizes the interface between the stem and the bone, resulting in increased micromotion that produces rapid fatigue failure of the transfixation screws placed through the flange into cortical bone. The wear debris associated with the failed screws, combined with prosthetic micromotion, results in a spiral of increasing loosening. Eventually, the stem fixation fails. Despite extensive modification of the flange positioning and the number of transfixation screws, this design remains inferior to the MRS produced in the United States.

An unexpected benefit of extracortical bone fixation has been the clinical observation that osteolysis surrounding the cemented stem does not appear in regions immediately adjacent to the porous coating on

the body. This effect, termed the "biologic pursestring", is believed to occur because tissue that has adhered to the porous coating isolates the stem–cement–bone complex from the wear-debris-laden fluid that surrounds the joint and prosthetic body. In addition to supporting laboratory and clinical data implicating polyethylene wear-debris in the genesis of osteolysis, this observation indicates that a circumferential porous coating is a necessary feature for any prosthetic bone implant. Accordingly, the MRS features circumferential beads, that permit bone grafting for extracortical fixation and stress reduction of the cemented stem, as well as ingrowth of fibrous tissue to prevent osteolysis and loosening of the cemented stem.

Selection of an appropriate joint mechanism is critical both to the functional outcome and the long-term durability of an endoprosthesis. A prosthetic joint must provide stability, particularly in situations with significant resection of soft-tissue constraints (ligaments, capsules). Reconstruction of the hip joint is readily accomplished by means of a bipolar hemiarthroplasty, given the inherent stability of a ball-and-socket joint. Dislocation can be prevented through meticulous reconstruction and/or augmentation of the hip capsule. Because the majority of these patients are young, there are few indications for total hip replacement. Tumors requiring resection of the acetabulum may be reconstructed with a saddle endoprosthesis.

Replacement of the knee is more difficult, largely because of the unique anatomical and biomechanical features of this joint. Early prosthetic designs consisted of a simple hinge mechanism (Walldius, Guepar) or a constrained ball-and-socket design (Sphero-centric). However, highly constrained systems such as the early total knee designs, have a high incidence of failure related to loosening or breakage. The most probable reason is that normal knee biomechanics include gliding translations and rotations that cannot be duplicated by a simple hinge (Figure 25.5). The original HMRS prosthesis used a simple hinge joint supported by polyethylene bushings. The high incidence of bushing failure noted in clinical series supports this assumption. Accordingly, the current MRS relies upon the Kinematic rotating hinge design. This semiconstrained mechanism permits three major degrees of freedom (superior/inferior translation, internal/external rotation, and flexion/extension), one minor degree of freedom (five degrees of varus/valgus rotation or tilt), and constraints on medial/lateral and anterior/posterior translation. This mechanism reproduces the restraints provided by the cruciate and collateral ligaments, and creates a very stable knee, even when these primary restraints of the knee have been totally resected. Preservation of the four degrees of freedom

helps protect the polyethylene bushings that support the primary axle and reduce torques transmitted to the prosthetic/bone junctions.

FUNCTIONAL RECONSTRUCTION AND ANATOMIC CONSIDERATIONS

The functional outcome of an endoprosthetic replacement is directly related to the amount of functional muscle preserved at the time of surgical resection. This simple observation can be used to project an outcome for an individual patient prior to surgery. For example, a large high-grade sarcoma of the proximal humerus requires an extra-articular resection of the shoulder, sacrificing the entire rotator cuff, in conjunction with sacrifice of the axillary nerve to achieve a true oncologic wide resection. Given the magnitude of this resection the optimal outcome is a stable painless shoulder that permits functional use of the elbow, forearm, wrist, and hand. This is accomplished by combining a static suspension of the prosthesis from the remaining scapula and clavicle, with a dynamic suspension composed of local muscle transfers that stabilize the shoulder and facilitate internal rotation (i.e. transfer of the pectoralis major). In contrast, the resection of rare low-grade sarcoma or a palliative resection for metastatic disease can be safely accomplished by performing a marginal resection, preserving many of the critical functional elements around the shoulder. Shoulder function will be much greater if the means of powering the shoulder are preserved.

These same principles hold true for endoprosthetic replacement of any portion of the skeleton, and are independent of the design of the prosthesis. However, prosthetic design can help facilitate the overall outcome in several key aspects. First, exact duplication of the skeletal anatomy being reconstructed is not necessary to achieve an excellent outcome. On the contrary, it is preferable to minimize prosthetic protuberances (such as a faux greater trochanter for a proximal femoral replacement) so that a better closure can be achieved with the remaining soft tissues following resection. Minimization of the medial/lateral diameter of the components around the knee can also greatly facilitate soft tissue closure of the knee mechanism. Second, functional groups have traditionally been reattached by making drill holes to pass sutures through the prosthesis. The loops allow the surgeon to pass sutures if desired, but also permit a tendon to be passed through the loop so that it may be sewn directly to itself. The positioning of these loops is therefore a critical design feature. Again, exact mimicry of the skeletal anatomy fails to account for tissue loss during the resection process; this must be considered in the placement of

the attachment sites. The soft-tissue attachment may be further reinforced by adding bone graft to the site, where a porous coating can permit ingrowth of tissue. Other methods of soft-tissue attachment, such as spiked screw plates designed to firmly hold a tendon, are under investigation.

The use of a polished smooth stem inserted with bone cement using "third-generation" cement techniques (i.e. vacuum mixing to reduce porosity, pressure injection into a prepared canal with an inserted cement restrictor, and centralization of the stem during the insertion process), remains the gold standard for fixation of an endoprosthesis. This is particularly true in patients undergoing adjuvant treatments such as systemic chemotherapy or radiation that can inhibit bone growth. The major advantage of cementation for oncologic patients is that it produces the immediate rigid and painless fixation, which reduces the need for postoperative protected weight-bearing or bracing and permits early functional rehabilitation. This has a tremendous positive physical and mental impact on the patient. Cement also conforms to the biologic and stem geometry, maximizing the contact between the stem and bone. In addition, the injection of cement can strengthen and compensate for the reduced mechanical properties of bone, which may be significantly weakened. Osteoporosis from disuse and osteopenia from poor nutritional intake, increased metabolic wasting, and an altered hormonal milieu, frequently occur in patients with chronic disease as well as in those receiving chemotherapy. Certain patients may, however, be candidates for "biologic fixation", such as a porous-coated press-fit stem.¹¹ For example, a young, active patient with excellent bone stock undergoing revision surgery or resection of a low-grade tumor for which adjuvant treatment is not indicated may benefit from the long-term fixation that a press-fit stem may offer. One advantage of a system such as the MRS is that a simple, customized stem that matches a patient's unique anatomy may be readily manufactured and used in conjunction with the other modular parts of the system.

STAGES OF LIMB-SPARING SURGERY

The three stages of a limb-sparing procedure are as follows:

1. tumor resection;
2. skeletal reconstruction; and
3. soft-tissue coverage and muscle transfers to restore function.

The majority of this textbook deals with the surgical techniques required to perform a safe oncologic resection of a primary bone sarcoma. Successful functional

reconstruction of the resulting defect consists of two separate but dependent stages. The first is the implantation of an endoprosthesis, which restores the length and stability of the skeleton. The second is the soft-tissue reconstruction that is required to cover the prosthesis and restore function to the joint.

The endoprosthesis is implanted in a systematic fashion. By rigorously following the same steps the surgeon can achieve a reliable, long-lasting reconstruction. Meticulous attention to soft-tissue reconstruction is vital to reducing the incidence of wound breakdown and secondary prosthetic infection.

GUIDELINES FOR SKELETAL RECONSTRUCTION (STAGE 2)

Endoprosthetic Selection and Implantation

Following resection of a segment of bone, the specimen is carefully measured in order to select the best-fitting prosthetic components. Trial components are provided to enable a rapid comparison with the specimen, as well as to perform trial reductions prior to selection and assembly of the final prosthesis. The following steps are necessary to prepare the intramedullary canal for stem insertion. Note that the selection of the stem diameter is dependent upon the anatomy of the canal, which is sequentially reamed in order to accommodate the largest-diameter stem possible.

1. Frozen section evaluation of the marrow contents by a skilled musculoskeletal pathologist is required to ensure that no tumor cells are present within the bone marrow prior to the preparation of the intramedullary canal. After insertion of a guidewire the canal is sized and enlarged with a flexible intramedullary reamer.
2. After the stem diameter has been selected, a facing reamer is inserted into the canal to machine a curved radius in the free end of the bone. This radius is designed to match the radius of curvature at the stem/body junction of the prosthesis, and thereby maximizes the fit between the prosthetic body and the bone.
3. The reamed canal is cleaned. A pulsatile lavage and an intramedullary brush helps remove clots and bone debris. A plastic cement restrictor is inserted to assist in pressurization of the cement at the time of implantation. The canal is packed to minimize bleeding during the remaining preparatory steps.
4. The adjacent joint surface is then prepared to accept the prosthesis. The steps required vary by anatomic site and are outlined in the following section.
5. A trial prosthesis is assembled and inserted. The surgeon checks for implant position, joint stability,

limb length, and range of motion. Length discrepancies are corrected by removing additional bone using the facing reamer (for small adjustments), varying the size of the polyethylene component in the proximal tibia (for distal femoral replacements), or changing the body segment selected.

6. The final prosthesis is assembled on a back table using the assembly holders and impactors provided with the system. All Morse tapers must be completely clean and dry to ensure a mechanically sound interference fit.
7. Cementation of the canal and insertion of the assembled endoprosthesis is performed using third-generation techniques.
8. The final step prior to the soft-tissue reconstruction is the application of onlay bone graft for extracortical fixation. Autogenous bone graft (often taken from the adjacent joint surface) is positioned across the prosthetic bone junction and tied in place using a large-diameter Dacron tape.

Preparation of the Adjacent joint by Anatomic Site

The adjacent joint surface must be prepared to accept the endoprosthesis prior to assembly of the final component. The preparation process varies with the anatomic location, as described below.

Shoulder (Proximal Humerus)

The majority of patients treated for tumors of the proximal humerus undergo an extra-articular resection of the shoulder in order to ensure an adequate surgical margin.¹² A combination of static and dynamic restraints around a unipolar prosthetic head provides stability for the joint. Selection of the head diameter is based on the local anatomy. Large-diameter Dacron tapes are used to suspend the prosthesis from the remaining scapula and/or clavicle (static restraint). Multiple muscle transfers, including the pectoralis major muscle, are performed to achieve prosthetic coverage and joint stability.

Proximal Femur (and Total Femur) (Figure 25.7)

Bipolar hemiarthroplasty is the preferred method of reconstruction for the hip. Resection of the surrounding tissue of the acetabulum significantly denervates the acetabulum, and creates a painless hip, even in young, very active, patients. Conversion to a total hip is possible, but rarely indicated. The bipolar head size is chosen after measurement of the acetabulum (either with sized acetabular trials by direct measurement of

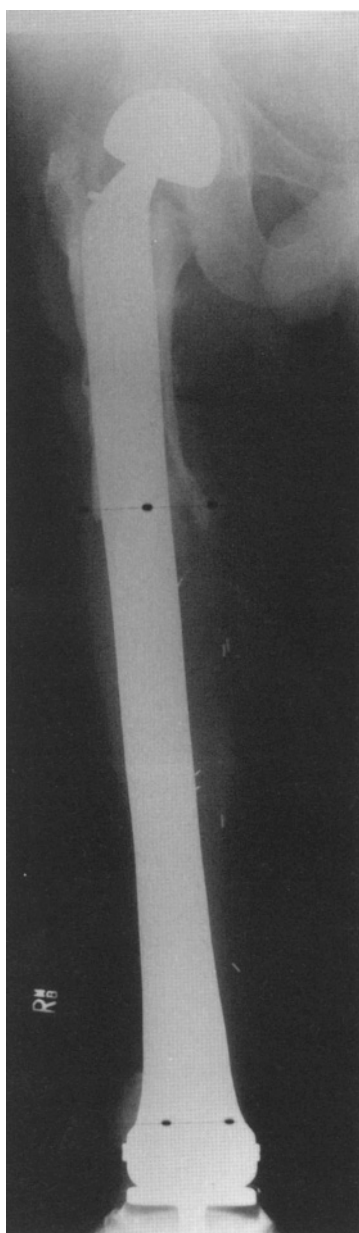


Figure 25.7 Radiograph of a large total femoral custom prosthesis with a bipolar hip component and a Kinematic rotating hinge prior to the use of the modular design (1988).

the diameter or of the excised femoral head). Following implantation of the prosthesis, joint stability is enhanced by transfer and myotenodesis of the psoas and the external rotators. Dacron tapes are placed around the prosthetic neck, where they act as static restraints. This method virtually eliminates the risk of dislocation in the postoperative period.

Distal Femur (and Total Femur) (Figure 25.8)

The top 1 cm of the tibial plateau is removed with an oscillating saw (a neutral cut without posterior slope) and saved for the extracortical onlay bone graft. Trial components are used to select the largest tibial component that fits on the proximal tibia with minimal medial–lateral overlap. (Overlap must be avoided to facilitate the soft-tissue closure over the prosthesis.) The tibial canal is prepared with a guide placed over the plateau to create a distal bone plug and proximal box to accommodate the stemmed polyethylene tibial-bearing component. Following trial reduction of the selected components the tibial insert is cemented into place using third-generation cement techniques.

Proximal Tibia (Figure 25.9)

The femoral condyles are resurfaced using a technique similar to that used for a total knee replacement. The femoral canal is opened with a reamer to allow for insertion of an intramedullary guide. A distal femoral cut is performed to remove 8 mm of the condyles. Anterior and posterior chamfers are created with an oscillating saw or a high-speed burr to accommodate the standard-sized femoral component. After trial reduction this component is cemented into place using third-generation cement techniques.

GUIDELINES FOR SOFT-TISSUE RECONSTRUCTION (STAGE 3)

The basic goals of the soft-tissue reconstruction are to provide adequate coverage of the prosthesis and restore muscle power and joint stability. A variety of local and regional muscular rotation flaps must be performed to maximize functional outcome and ensure adequate coverage of the prosthesis. Meticulous attention to handling the soft tissues and preserving the regional blood supply is essential at this step. Complete muscular coverage of the prosthesis minimizes the risk of periprosthetic infection related to superficial wound breakdown (marginal necrosis) that occasionally occurs following the creation of large flaps during an oncologic resection. Muscle transfers also improve stability of the reconstructed joint, and restore useful joint function. Aggressive mobilization of the remaining muscles crossing a given joint, as well as specific muscular rotational flaps, permits the surgeon to achieve all of these goals without creating free flaps.

To provide functional power to the limb, soft tissue must be attached to the prosthesis. This entails attaching the major tendons to the prosthesis (using the provided metal loops) and creating a musculotendinous cuff around the body of the prosthesis. In addition,

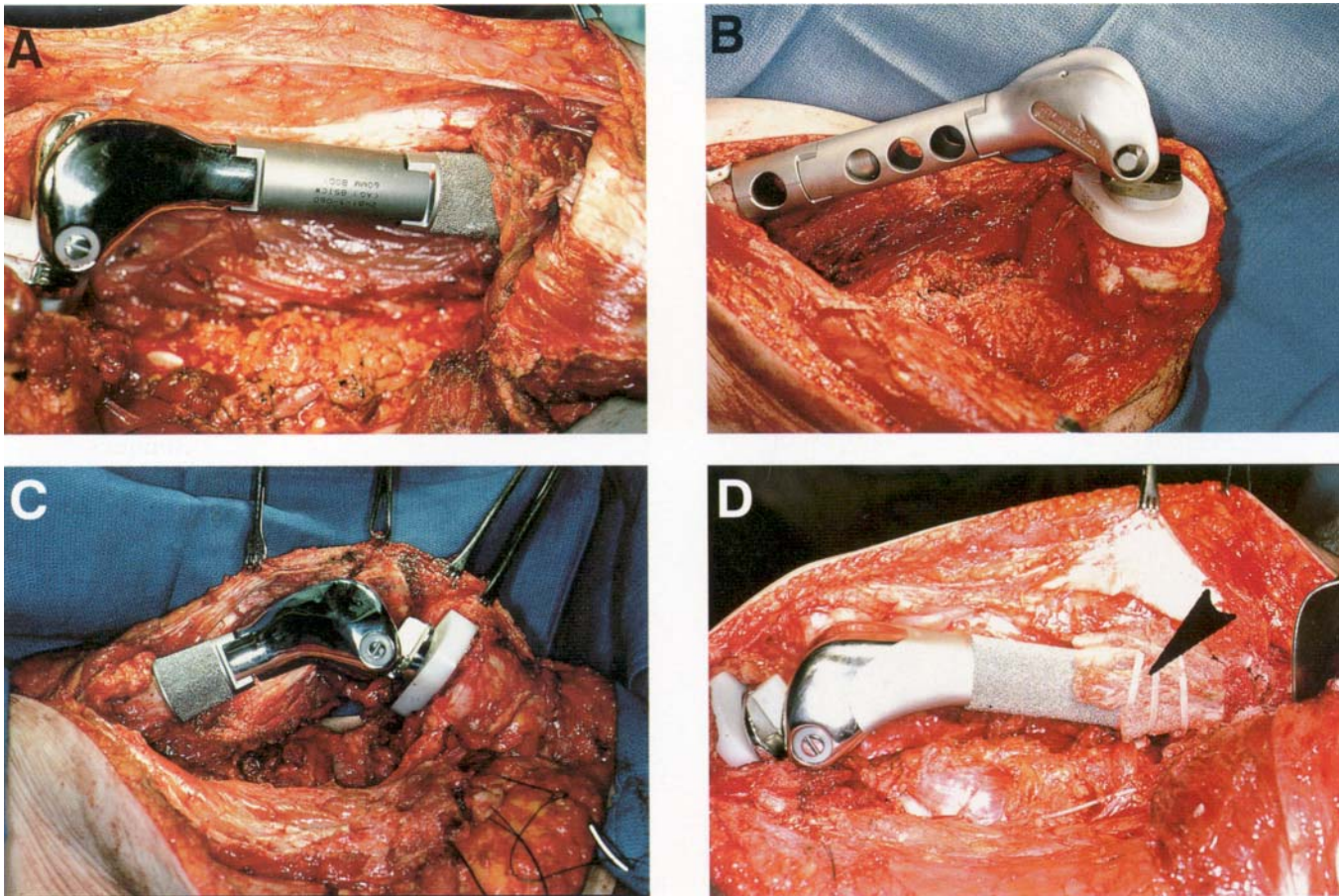


Figure 25.8 Intraoperative photographs of a distal femoral replacement. (A) A completely assembled distal femoral prosthesis (Modular Replacement System, Stryker Howmedica Osteonics, Inc., Allendale, NJ). (B) Trial prosthesis to determine the appropriate length and tension. Note a trial prosthesis of the Modular Replacement System has large holes in the body and stem to avoid mistaken implantation. (C) Distal femoral replacement without the use of a body. This is utilized for small segmental resections and is required for some Stage III giant cell tumors and small (Stage I) intra-osseous sarcomas. (D) Intraoperative photograph of a custom prosthesis used prior to 1988 with a large area of the body being porous coated. Note the attached bone graft to the porous coating with Dacron tape (arrow) is to permit extracortical fixation. New bone formation is usually visualized radiographically between 8 and 16 weeks postoperatively.

restoration of proper limb length helps ensure stability of the reconstruction. As noted previously, the prosthesis has a beaded porous coating at sites of important tissue attachments. The porosity allows both for bone and fibrous ingrowth: a new tendon–bone junction is created by adding bone graft between the porous surface of the prosthesis and the tendon which is held firm to the prosthesis with Dacron sutures.

Details of common muscle transfers are provided elsewhere in this textbook. These routine muscle transfers include the following:

1. Shoulder: transfer of the pectoralis major and latissimus dorsi muscles covers and dynamically stabilizes
2. Hip: the psoas and external rotators are transferred to create a pseudocapsule around the prosthetic head. This capsule is reinforced with circumferential Dacron tapes to prevent dislocation. Reattachment of the abductor muscles is necessary to minimize the Trendelenberg lurch in the postoperative phase. This limp improves over time with strengthening of the abductors.
3. Knee: 25% of distal femoral replacements and all proximal tibial replacements require rotation of a gastrocnemius muscle (typically the medial head) to

a proximal humeral prosthesis. Dacron tapes are used to statically suspend the prosthesis from the scapula.

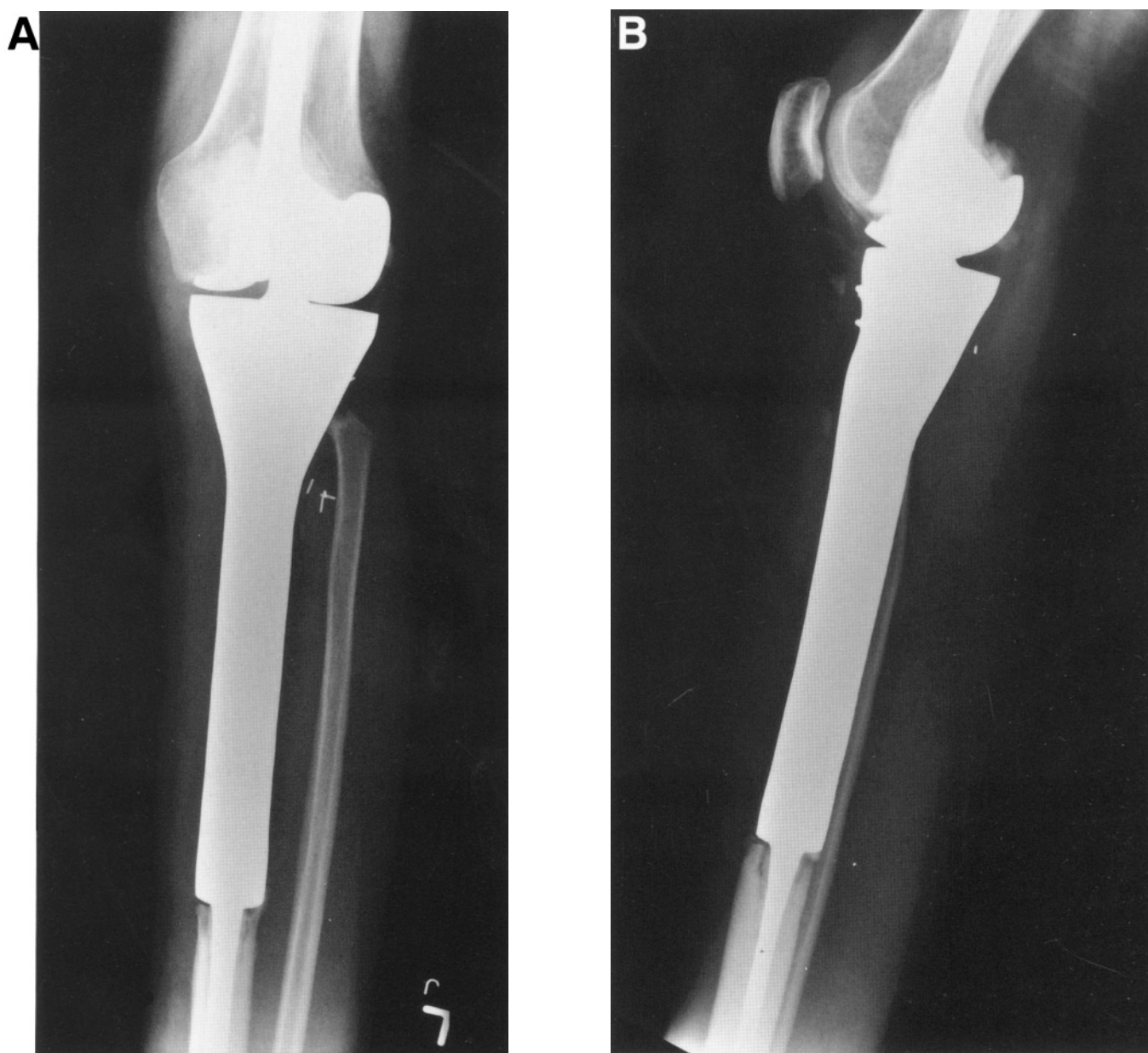


Figure 25.9 Custom segmental prosthesis with a spherocentric knee component utilized prior to the early 1980s for the proximal tibia. (A) The anterior–posterior view. (B) Lateral view. Note that this is a spherocentric knee design and not a rotating hinge. This was the original design utilized for knee replacements during the 1970s. A rotating hinge knee became available during the early 1980s.

repair the soft-tissue defect following resection of a tumor around the knee. This local flap is incorporated into the reconstruction of the patellar tendon in patients undergoing proximal tibial replacements.¹³

Final closure of the wound may be jeopardized by skin loss following resection of a biopsy tract. Patients with very large tumors generally have extra skin because the growing tumor acts as an internal skin stretcher. This

extra skin can be rotated to facilitate the wound closure. Excess skin along the incision should be excised to avoid marginal wound necrosis related to regional devascularization during the creation of large flaps. To avoid pressure-induced ischemia, patients with tight skin closures are best served by leaving the skin open and performing a primary or secondary split-thickness skin graft. Patients must be maximally elevated in the postoperative phase to reduce swelling that can

jeopardize the wound closure. Use of large-bore closed suction drains and correction of any postoperative coagulopathies is necessary to prevent hematomas. Patients who develop hematomas or wound breakdown require aggressive treatment in the operating room to prevent secondary infection of the endoprosthesis.

CLINICAL RESULTS FOLLOWING ENDOPROSTHETIC REPLACEMENT

Prosthetic survival has improved dramatically since the development of advanced surgical techniques, better prosthetic designs, and modern manufacturing techniques. Results of some early custom prostheses were disappointing, leading many surgeons to use allografts or other methods of reconstruction. More recently, as high rates of allograft complications have been reported, there has been increasing interest in the new generation of endoprostheses.

Complications are not uncommon with any type of limb-sparing procedure. The majority of these patients have altered immune systems from chronic disease, chemotherapy, and malnutrition. Many patients are anemic and have clotting abnormalities, including thrombocytopenia. Long-term indwelling catheters, used for the administration of chemotherapy, may cause a high incidence of line infections, that can jeopardize an endoprosthetic replacement through hematogenous spread of bacteria. The local anatomic location of a tumor may disrupt the venous and lymphatic drainage of the extremity during resection, leading to venous stasis, swelling, and lymphedema. This can quickly result in flap necrosis during the postoperative period. Secondary infection and eventual amputation may be the result. Finally, oncologic complications, including local recurrence of tumor or tissue necrosis from radiation, may result in failure of a limb-sparing procedure.

Complications specific to endoprosthetic reconstruction may be related to mechanical or biologic factors. Prosthetic fracture, dissociation of modular components, fatigue failure, and polyethylene wear may be encountered. Improved designs and metallurgy can significantly reduce the incidence of these problems (Figure 25.10). Our experience with more than 150 MRS implants over the past 12 years has revealed no stem fractures, body fractures, or taper dissociation. Polyethylene wear does occur, but less than 5% of patients with bushings in the rotating hinge mechanism have required exchange of these components.

Nonmechanical (biologic), failure of an endoprosthesis may occur as a result of aseptic loosening, or fracture of bone around the prosthesis. Joint stability is

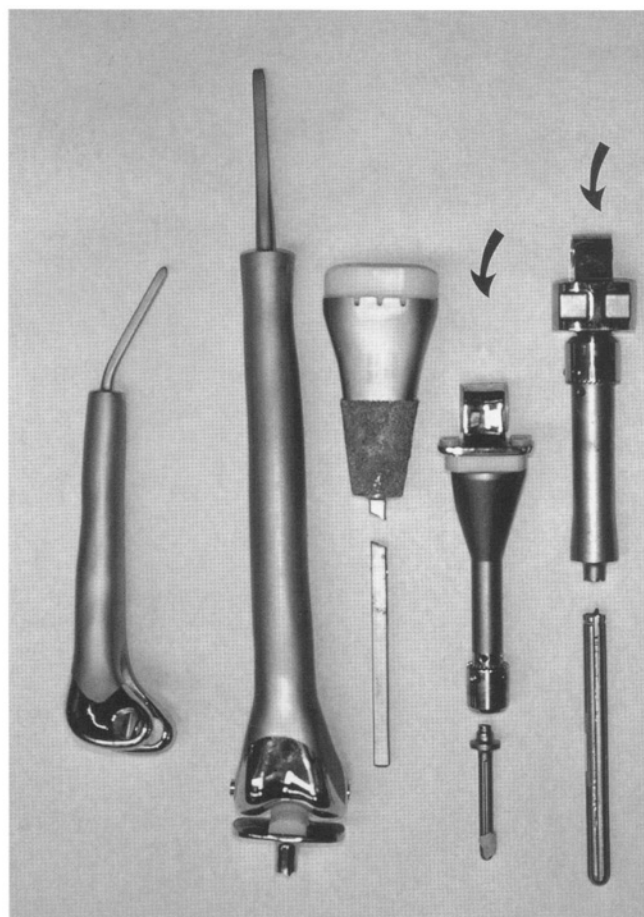


Figure 25.10 Composite photograph showing failures of several different prosthetic devices utilized during the 1980s and the various modes of failure. The most common mode of failure was either stem breakage or bending. Today, stems are heavily forged, have a curved transition at the junction with the prosthesis and are rarely less than 9 mm in diameter. Arrows = expandable prostheses with small stems used in young children.

no longer a problem. Moreover, the use of circumferential porous coating has dramatically reduced the incidence of aseptic loosening in our patients. Surgical technique, as well as the use of cemented stems, has prevented periprosthetic fractures during surgery. The few patients who have developed fractures as a result of blunt trauma (falls, auto accidents) have been treated successfully with casting and protected weight-bearing.

ENDOPROSTHETIC SURVIVAL

The majority of published United States series looking at the survival of endoprosthetic reconstructions are based on small series of custom components implanted

in the late 1970s and early 1980s. These include the following:

1. Chicago: 66% 10-year survival for distal femoral replacements (DFRs).¹⁴
2. England: 64% 7-year survival rate for DFRs.¹⁵
3. New York: 89% proximal femur, 59% distal femur, 54% proximal tibia.¹⁶
4. Washington: 83% 5-year and 67% 10-year survival for tumors at all sites.¹⁷

A more modern series was based upon experience with the HMRS system in Europe. Long-term data for the distal femoral replacement have been disappointing; an overall complication rate of 55%, a mechanical failure rate of 6% for stem breakage, and 42% polyethylene failure after a follow-up of 64 months¹⁸. As a result this particular system was never approved for use in the United States.

Our experience with the current-generation MRS has been very gratifying. Since its introduction in the 1980s, over 150 implants have been used at our center. Results of the first 100 prostheses, which have been followed for a minimum of 2 years, are summarized in Table 25.1.

For this series, "failure" was defined as removal of the prosthesis for any reason. Most notably there have been no mechanical failures to date involving the stems, bodies or tapers. All the prostheses that failed were the result of periprosthetic infection, at a 7% rate. Although this is significantly higher than the infection rate associated with total joint replacement, the majority of these patients were immunocompromised as the result of chemotherapy treatments. The rate of polyethylene bushing failure has been approximately 5%.

FUTURE DIRECTIONS FOR ENDOPROSTHETIC RECONSTRUCTION

The current MRS prosthesis has greatly facilitated limb-sparing surgery following resection of bone sarcomas.

Table 25.1 Results of the first 100 MRS

<i>Site of prosthesis (no.)</i>	<i>Survival at median follow-up</i>	<i>Kaplan–Meier survival at 10 years</i>
Distal femur (48)	90.7% at 63.0 months	90%
Proximal humerus (22)	98% at 77.8 months	98%
Proximal femur (15)	100% at 58.8 months	100%
Proximal tibia (13)	78% at 61.7 months	78%
Total femur (2)	100% at 25.4 months	
<i>All sites (100)</i>	<i>88.2% at 64.4 months</i>	<i>88 %</i>

Its success has expanded the indications for endoprosthetic reconstruction to include bone defects for nononcologic problems. Increasing experience with this system for salvage of failed total joint replacements, chronic nonunions of fractures, and reconstruction following radical resection of osteomyelitis has shown that the proven concepts of limb-sparing surgery can be easily applied to many other clinical situations.

Current research to improve the performance of the MRS prosthesis is focusing on improved work on advanced bioactive coatings, alternative methods of stem fixation, and improved methods of attaching soft tissue. Continued work on improved metallurgy and polymers, particularly with the introduction of cross-linked polyethylene, is expected to improve the durability of the MRS. Although future advances in tissue engineering hold the promise of artificially engineered bones, we expect that endoprosthetic reconstruction will remain the implant of choice of orthopedists for many years to come.

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26

Pelvic Resections (Internal Hemipelvectomies)

Jacob Bickels and Martin Malawer

OVERVIEW

Internal hemipelvectomies involve resection of part or all of the innominate bone with preservation of the extremity. This chapter will describe the surgical technique of resection of the ilium (Type I pelvic resection) and the pubic region (Type III pelvic resection). These resections do not violate the hip joint and minimally compromise the stability of the pelvic girdle, and therefore do not require reconstruction. Detailed preoperative evaluation and meticulous surgical dissection are crucial because of the close proximity of the pelvic girdle to major blood vessels, nerves, and internal organs in these regions. The surgical technique of Type II (periacetabular) resection is described in Chapter 28.

INTRODUCTION AND ANATOMIC CONSIDERATIONS

The pelvic girdle is a common location for primary bone sarcomas and metastatic lesions with the periacetabular region being the most common location, followed by the ilium and the pubis. Hemipelvectomy, the classic treatment for these lesions, has been associated with dismal functional and psychological outcomes. Improved survival of patients with musculoskeletal malignancies, and refinements in surgical technique, have allowed the execution of limb-sparing procedures in these situations. Local tumor control is good, as is the probability of a functional extremity. Internal hemipelvectomies, which involve resection of part or all of the innominate bone with preservation of the extremity, are now a reliable surgical option in the treatment of primary bone sarcomas, benign-aggressive lesions, and metastatic tumors of the pelvic girdle.

Detailed preoperative evaluation is necessary in order to evaluate the bony and soft-tissue extents of the tumor and their relation to the major blood vessels, nerves, and pelvic viscera. The complex anatomy of the pelvic girdle, and the close proximity of the major neurovascular bundle and pelvic cavity, necessitate wide exposure of the surgical field. No attempt is made to resect a tumor through a limited incision; this might result in injury to a major structure and compromise the oncologic quality of the surgery.

The classification of internal hemipelvectomies is based on the resected region of the innominate bone, from posterior to anterior: Type 1 – ilium; Type 2 – periacetabular region, and Type 3 – pubis. En-bloc resection of the ilium and sacral ala is classified as an extended Type 1 or Type 4 resection (Figure 26.1).

Resection of the ilium can be partial or complete; only a segment of the iliac wing or the entire ilium can be resected. Stability of the pelvic girdle is not impaired after partial iliac resection because a rim of bone still bridges the periacetabular region and the sacrum. Complete iliac resection, on the other hand, impairs pelvic girdle stability because the space created between the acetabulum and the sacrum allows upward migration of the lower extremity upon weight-bearing. However, the extent of that migration is not significant because a contralateral, stiff sacroiliac joint and the extensive scar formation in the surgical site prevent excessive tilting. As a result, limb-length discrepancy of not more than 2 cm is observed in most cases and can be effectively treated with ipsilateral shoe lift. It is therefore a matter of controversy whether to reconstruct the retroacetabular defect or not.

The inner aspect of the ilium is covered by the iliacus muscle, which originates from the iliac crest. The iliacus is “pushed” by a growing bone sarcoma and serves as a

barrier to direct extension of a tumor to the pelvic viscera. The same is true for the gluteus medius muscle, which lies against the outer table of the ilium. When resection of the ilium is performed for a benign-aggressive lesion, both muscles can be spared. However, when the resection is performed for a primary bone sarcoma or a metastatic lesion, both of which commonly break through the inner and outer table, the portion of the iliatus and gluteus medius muscles which lies against the ilium must be resected en-bloc with the tumor. It is important to try to spare as much substance of the gluteus medius muscle as possible because it will serve for reconstruction of the abductor mechanism and soft-tissue coverage of the pelvic cavity.

Isolated resections of the pubis are rare; in most cases these are performed in conjunction with resection of a large periacetabular tumor. As opposed to tumors of the ilium, there is no muscular layer between tumors of the pubis and the pelvic organs; the urinary bladder and urethra, which lie directly behind and under the symphysis pubis, are usually only a few millimeters from the growing edge of a bone sarcoma or directly invaded by metastatic carcinomas of the pubic region. Because of the relatively superficial location of the pubis, surgeons tend to assume that pubic resections are simple, and often try to approach a pubic lesion through an inadequate exposure. Wide exposure is essential in order to achieve wide margins of resection as well as for mobilizing the femoral vessels and nerve, bladder, and urethra, which are in close proximity to the pubis.

The pubis does not bear weight, which is transmitted directly to the lower extremities via the hip joints. The lack of one or two pubic bones has minimal impact on stability of the pelvic girdle because of the presence of intact sacroiliac joints. Reconstruction is therefore not indicated following resection of the pubis.

SURGICAL TECHNIQUE

Type I Resection

The patient is positioned in a semilateral position (45°). The utilitarian pelvic incision, that was described in detail in Chapter 10, is used; its ilioinguinal component is advanced medially to the symphysis pubis and its posterior arm is brought to the level of the sacroiliac joint (Figure 26.2).

All muscle attachments, with the exception of iliatus and gluteus medius which are resected en-bloc with the tumor, are removed from the iliac crest. The abdominal wall musculature, sartorius, and tensor fasciae lata are transected from the iliac crest and reflected away from the ilium. The rectus femoris muscle remains intact (Figure 26.3). The iliotibial band is transected from its

origin from the iliac crest and reflected posteriorly along with the gluteus maximus. Large fasciocutaneous flaps are raised and reflected medially and posteriorly.

The plane between the iliacus and the psoas muscle is developed with caution because the femoral nerve lies in that space. The psoas muscle and the femoral nerve are reflected medially and the iliacus muscle is transected through its substance (Figure 26.4). The external iliac artery, which lies against the lower margin of the ilium, gives no major branches along the inner table of the ilium and ligation of large blood vessels is therefore not required in Type I pelvic resection. Most tumors of the ilium break through the outer table and push the gluteus medius muscle laterally. The gluteus

medius muscle is transected through its substance, 2–3 cm distally to the inferior border of the tumor (Figure 26.5). It is important to try to save as much muscle belly as possible because it will be the major component in soft-tissue coverage of the pelvic content and will be necessary for reconstruction of the abductor mechanism.

Osteotomy of the ilium is performed, using a malleable retractor which is inserted through the greater sciatic notch, along the inferior border of the inner table, and out just underneath the anterior superior iliac spine, to protect the pelvic viscera (Figure 26.6). The ilium is transected along the dotted line, leaving the origin of the rectus femoris muscle and the roof of the

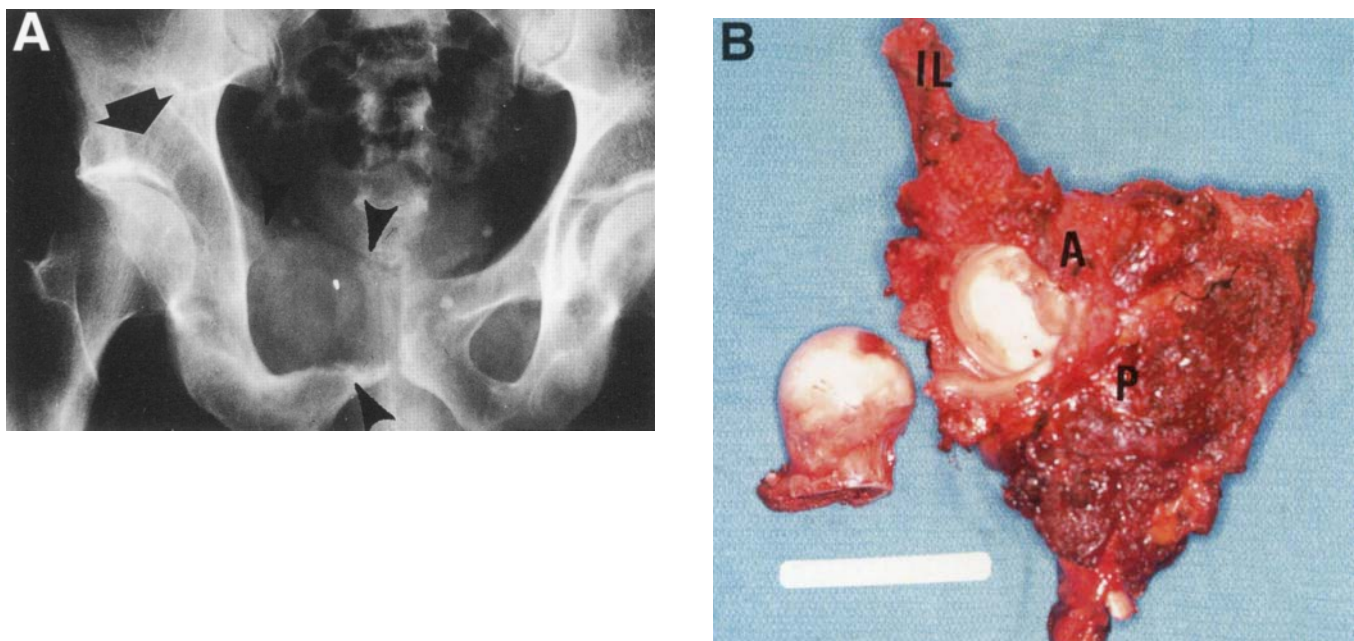


Figure 26.1 (see also following page) (A) Plain radiograph showing an extremely high-grade MFH arising from the superior and inferior pubic ramus involving the entire obturator foramen, pelvic floor, and medial and supra-acetabular aspect of the acetabulum (solid arrows). This was the first patient treated at our institution with a combined Type II/Type III resection in lieu of a hemipelvectomy. He received intra-arterial chemotherapy preoperatively (1988) and had median tumor necrosis of 95%. He underwent resection and reconstruction and remains free of local and disseminated disease at 12 years. (B) Gross specimen following Type II/Type III pelvic resection performed in 1988 (IL = portion of the ilium; A = acetabulum; and P = the entire pelvic floor including superior and inferior pubic ramus). (C) Gross specimen following a complete internal hemipelvectomy (Type I/Type II/Type III pelvic resection). IL shows portion of the ilium; A = acetabulum; SP = the superior pubic ramus, IP = the inferior pubic ramus and pubis. The femoral head is seen still attached by the ligamentum teres. It is our practice (for large periacetabular tumors) not to remove the femoral head separately. There is a small incidence of tumor spreading from the periacetabular region, especially the medial wall, through the ligamentum teres, into the synovium and femoral head. Therefore, we attempt to perform an extra-articular resection. (D) Radiograph of the resected specimen showing complete involvement of the hemipelvis. The defect superiorly was created by an open biopsy. (E) Gross specimen of a combination Type II/Type III pelvic resection. The acetabulum can be visualized and a large tumor mass involving the entire floor and the superior and inferior pubic rami was removed en-bloc. Type II/Type III pelvic resections are extremely difficult and can often be performed only following induction chemotherapy if there is a good response to the chemotherapy. (F) Gross specimen following a Type III pelvic resection. There is a large tumor mass arising from the obturator internus muscle (solid arrows). The symphysis pubis (SY) is seen. The medial wall of the acetabulum was not involved, but was the closest margin. In general, following a Type II or Type III pelvic resection for low- or high-grade sarcomas, radiation therapy is used postoperatively to avoid a local recurrence.

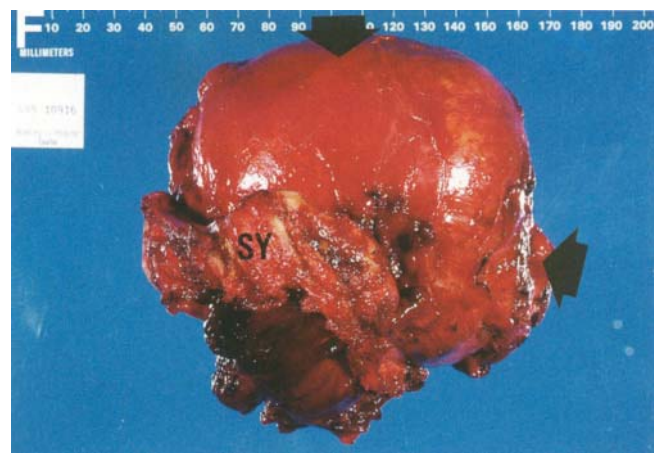
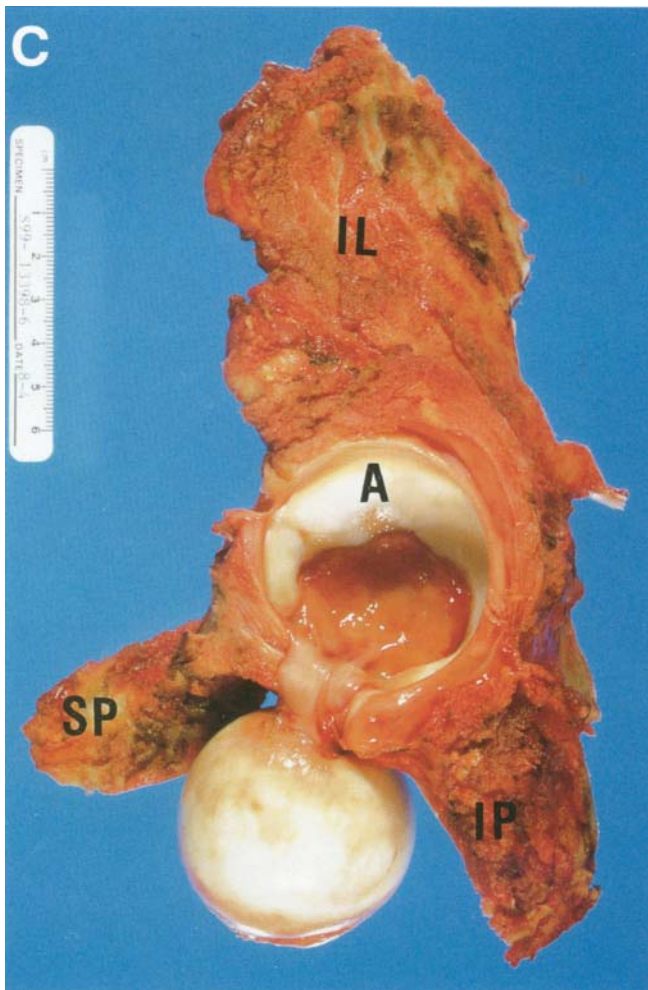


Figure 26.1C–F

acetabulum intact. Osteotomy of the posterior aspect of the ilium is then performed; a malleable retractor is positioned through the greater sciatic notch, along the posterior border of the ilium and in parallel to the ipsilateral sacral ala. The osteotomy is moving to the inside (Figure 26.6).

The most important component of soft-tissue reconstruction is the attachment of the proximal rim of

the gluteus medius muscle to the abdominal wall musculature. Even if the entire gluteus medius muscle was spared, the attachment of these two muscle groups, which are not anatomically connected, creates a significant tension, which can be reduced by placing the lower extremity in abduction. The suture line is reinforced with the tensor fasciae lata and sartorius muscles (Figure 26.7). Closure of the muscle layer must

be meticulously executed because poor healing and wound dehiscence will expose the abdominal and pelvic contents and will be difficult to manage.

The extremity is kept in balanced suspension for at least 5 days. An abduction brace is customized for the patient. Continuous suction is required for 3–5 days. Perioperative intravenous antibiotics are continued until the drainage tubes are removed. Postoperative mobilization with an abduction brace and weight-bearing as tolerated are continued for 3 weeks, by the end of which the abduction brace is removed.

Type II Resection

Resection of the acetabulum alone is termed a peri-acetabular resection. This is classified as a Type II pelvic resection. Tumors of the acetabulum are difficult to treat. Various techniques of reconstruction have been described, including: allografts, prosthetic replacement, ischiofemoral arthrodesis, and the saddle prosthesis.

The surgical technique of resection requires three osteotomies be performed: superior pubic ramus, ischium,

and supra-acetabular. The surgical approach utilizes the ilioinguinal incision as well as the retrogluteal approach.

Chapter 28 describes in detail the surgical technique and reconstruction of periacetabular (Type II) defects.

Type III Resection

The patient is positioned in a slight elevation of the ipsilateral hip. The ilioinguinal component of the utilitarian pelvic incision with a caudal extension is used (Figure 26.8). This incision allows exposure and mobilization of the femoral vessels, nerve, and bladder. The caudal extension of incision is used to expose the ischium, which is resected through the ischiorectal fossa when the resection is performed for a large pubic lesion.

Large myocutaneous flaps are raised. The spermatic cord is reflected medially. The inguinal ligament is transected from its pubic insertion and reflected laterally. The neurovascular bundle (femoral artery, vein, and nerve) is reflected laterally, exposing the origin of the adductor magnus and pectineus muscles, which is transected off the pubis and reflected distally. Using the

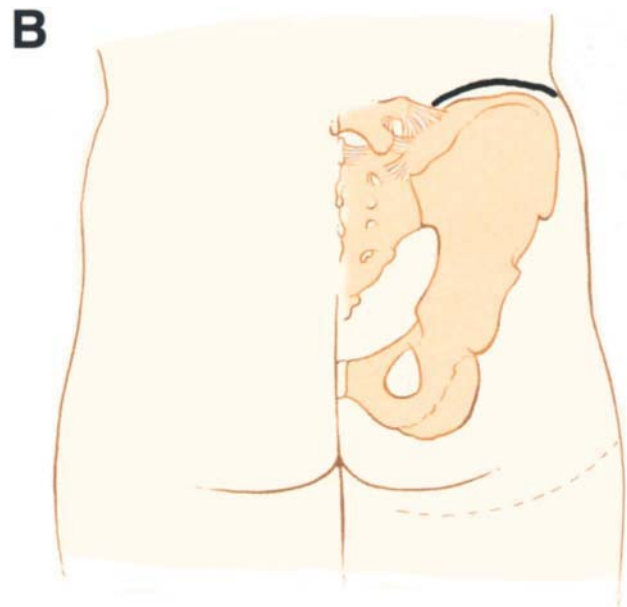
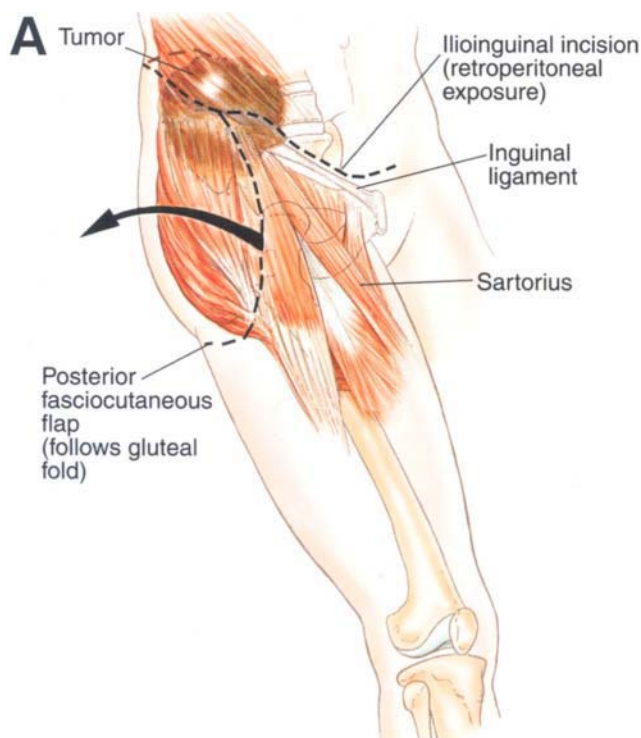


Figure 26.2 (A) Incision and surgical approach. The entire utilitarian incision is used for Type I (iliac) resection. The posterior fasciocutaneous flap exposes the entire retrogluteal area; the sciatic notch, the sciatic nerve, the abductor muscles and the hip joint. This approach provides a good exposure of the retroperitoneal space as well as the posterior retrogluteal area and permits a safe resection of the ilium. The ilioinguinal component is advanced medially to the symphysis pubis and, (B) posteriorly to the sacrum.

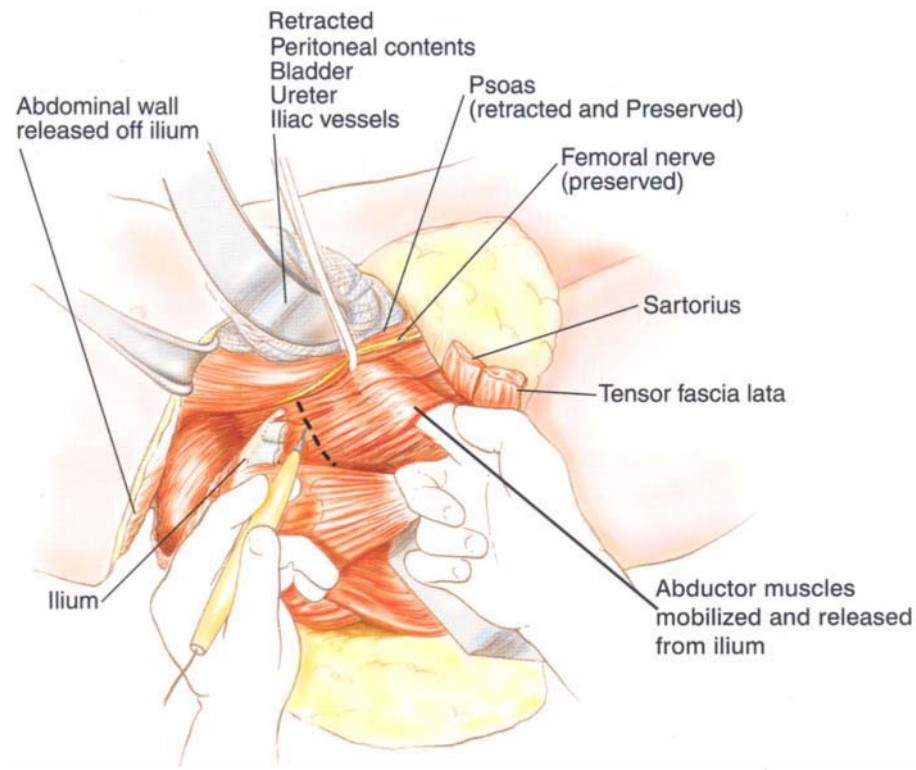


Figure 26.3 Posterior exposure and muscle releases. The abdominal wall musculature is transected off of the iliac crest. The sartorius and tensor fasciae lata muscles are transected from their tendinous and reflected distally. The rectus femoris muscle remains intact. Large fasciocutaneous flaps are raised and reflected medially and posteriorly. The iliotibial band is transected from its origin from the iliac crest and reflected posteriorly along with the gluteus maximus.

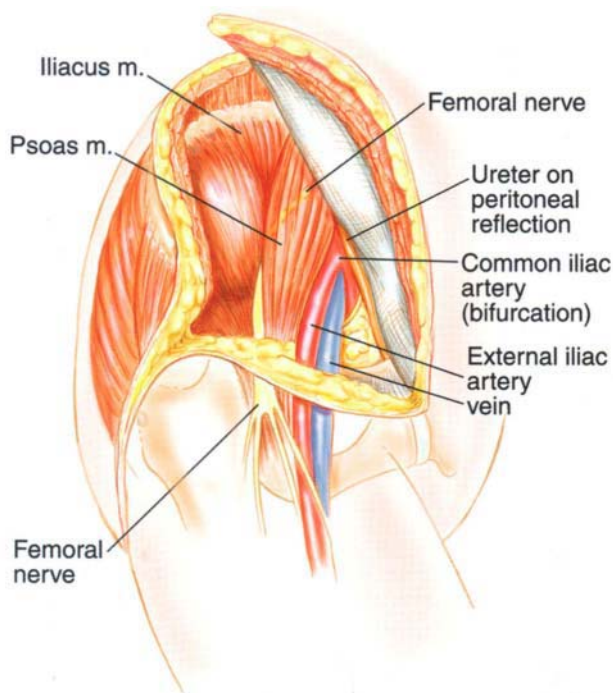


Figure 26.4 Anterior (retroperitoneal) exposure. The retroperitoneal space is easily exposed and explored through the ilioinguinal component of the incision. The plane between the iliacus and the psoas muscle is developed with caution because the femoral nerve lies in that space. The psoas muscle and the femoral nerve are reflected medially and the iliacus muscle is transected through its substance. The femoral nerve is preserved.

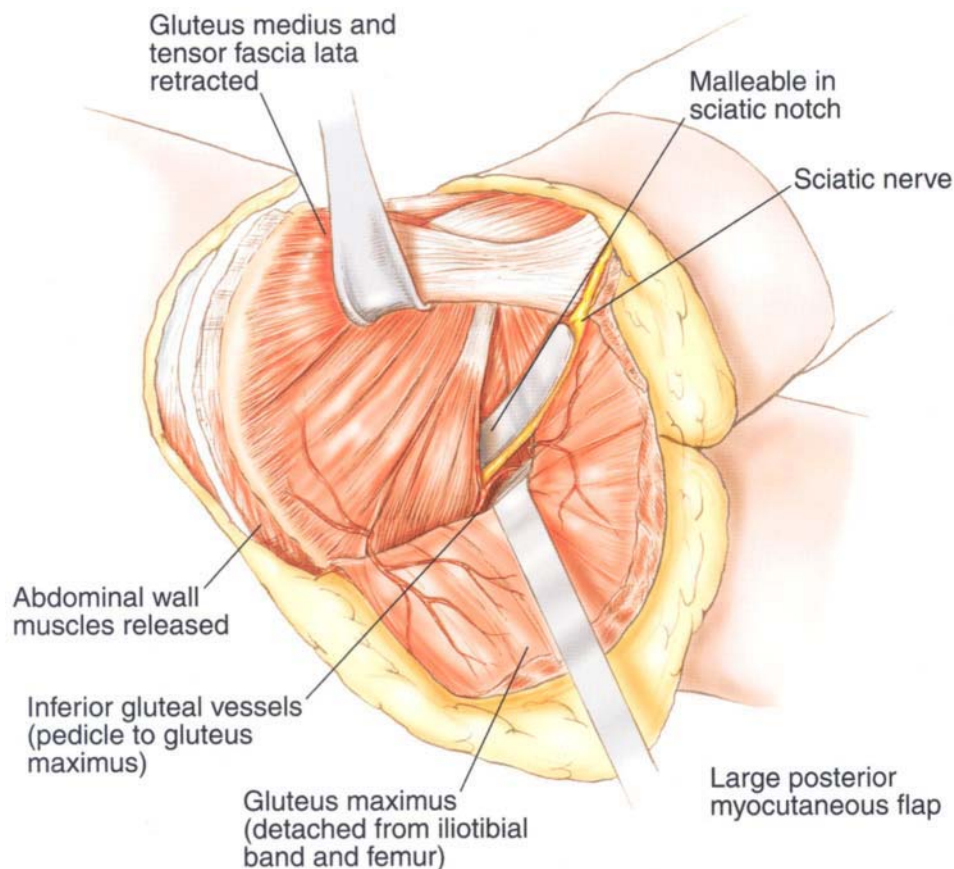


Figure 26.5 Posterior exposure and release of gluteal muscles. The retrogluteal area is exposed. The gluteus maximus muscle is released from the iliotibial band and from the femur and reflected posteriorly. The sciatic nerve is identified and preserved. All of the remaining abdominal muscles are released from the wing of the ilium. The gluteus medius muscle is transected through its substance, 2–3 cm distally to the inferior border of the tumor; it is important to try to save as much muscle belly as possible.

caudal component of the incision, the origin of the hamstrings, adductors, and gracilis is transected off the ischium and reflected distally. A first malleable retractor is placed behind the symphysis pubis, in front of the bladder. The second malleable retractor is placed behind the superior pubic ramus and in front of the inferior pubic ramus, medial or lateral to the ischium, depending on the required oncological margins (**Figure 26.9**). Osteotomy through the symphysis pubis and pubic rami is performed. It is important to smooth the

sharp bony edges, especially these which lie against the bladder.

Surgical wounds around the groin are notoriously known to be associated with a high incidence of dehiscence and infection. Meticulous wound closure with adequate drainage is therefore mandatory. Continuous suction is required for 3–5 days. Perioperative intravenous antibiotics are continued until the drainage tubes are removed. Postoperative mobilization with weight-bearing as tolerated is allowed.

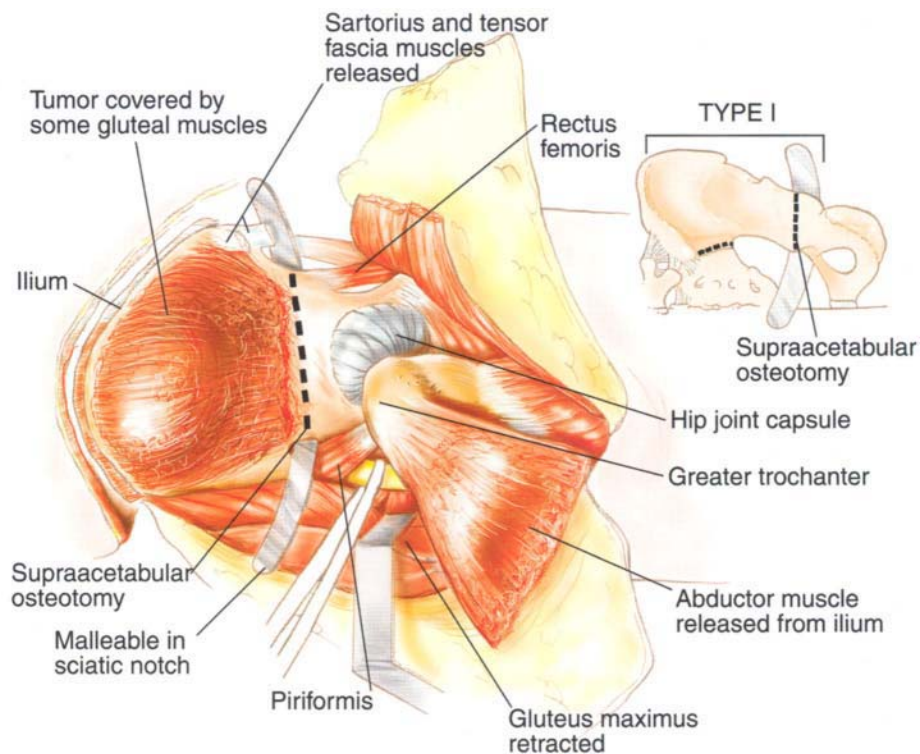


Figure 26.6 Supra-acetabular osteotomy and sacroiliac disarticulation. A malleable retractor is inserted through the greater sciatic notch, along the inferior border of the inner table, and out just underneath the anterior superior iliac spine, to protect the pelvic viscera. The ilium is transected above the hip capsule, leaving the origin of the rectus femoris muscle and the roof of the acetabulum intact. Care is taken not to enter the hip joint. (*Insert*) The sacroiliac joint is opened from within the pelvis. The iliac vessels must be mobilized and retracted before attempting to open the sacroiliac joint.

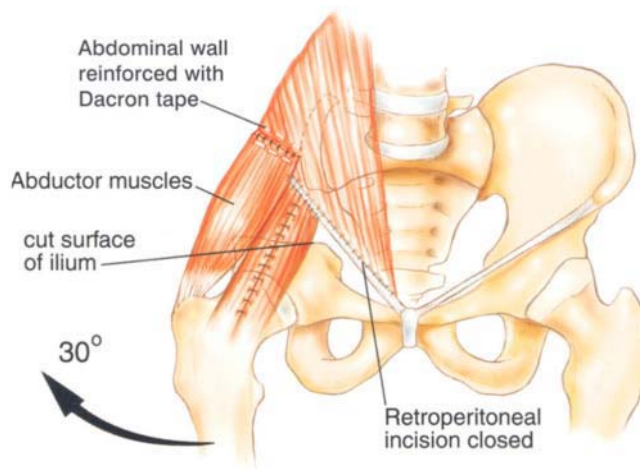


Figure 26.7 Soft-tissue reconstruction. The gluteus medius muscle is sutured to the abdominal wall musculature with the ipsilateral lower extremity in abduction. Dacron tape must be used to reinforce this reconstruction. The suture line is also reinforced by oversewing the tensor fasciae lata and sartorius muscles.

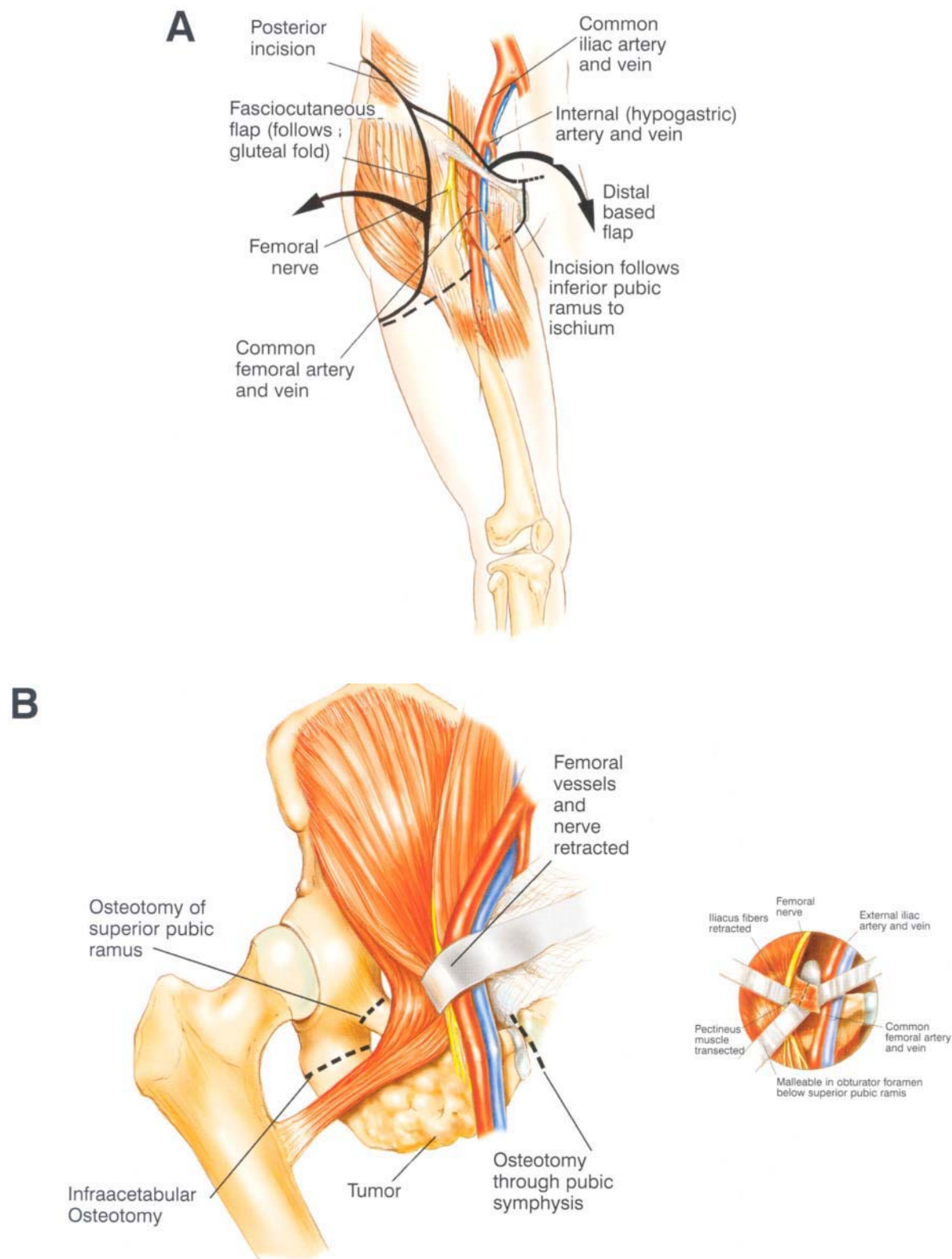


Figure 26.8 Incision. (A) The ilioinguinal component of the utilitarian pelvic incision with a modified perineal extension are used. The ilioinguinal component is advanced medially to the symphysis pubis. (B) Schematic of the three osteotomies required to remove the pelvic floor. A wide exposure of all three sites is required. The superior pubic ramus is approached through the anterior ilioinguinal incision. The spermatic cord is reflected medially. The inguinal ligament is transected from its pubic insertion and reflected laterally. The neurovascular bundle (femoral artery and vein) is retracted medially, exposing the origin of the pectineus muscle, which is transected to expose the underlying bone, the superior pubic ramus (*insert*). The superior pubic ramus is transected with a high-speed burr. Care must be taken to retract and protect the femoral vessels and the femoral nerve. Through the perineal component of the incision the origin of the hamstrings, adductors, and gracilis is transected off of the inferior pubic ramus and ischium and reflected distally.

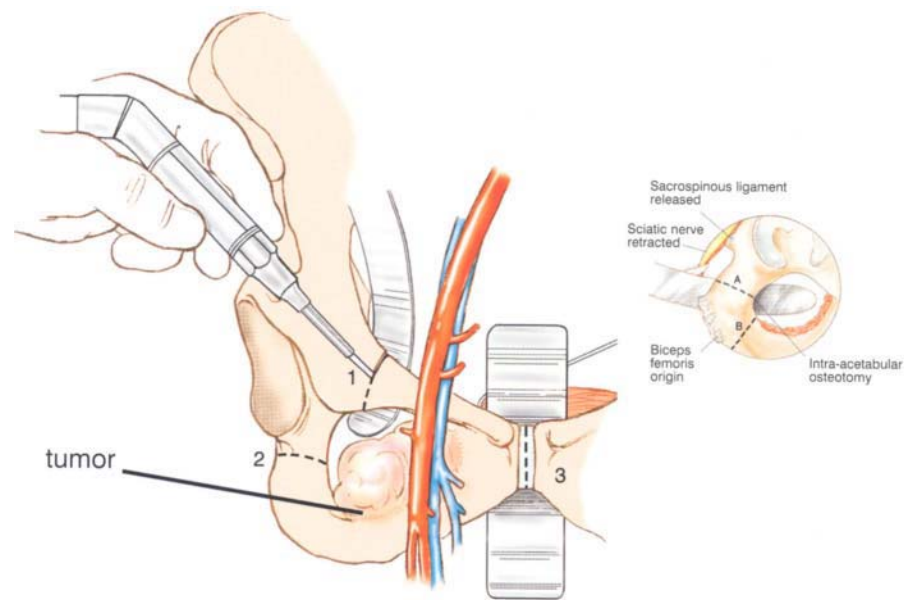


Figure 26.9 Transection of the symphysis pubis, superior pubic ramus, and ischial osteotomy. A malleable retractor is placed behind the symphysis pubis, in front of the bladder. This retractor protects the bladder and the urethra. The second osteotomy is performed either through the ischium or the inferior pubic ramus, depending upon the oncological need. A malleable retractor is placed behind the ischium. The ischium (or inferior pubic ramus) are identified by palpation and the attaching or overlying muscles are transected with a cautery. The quadratus femoris muscle must be transected as it crosses the ischium to provide exposure and correct placement of the retractors.

Sacrectomy

Constantine Karakousis and Paul Sugarbaker

OVERVIEW

Sacrectomy is used for the removal of pelvic tumors with sacral attachments or for chordoma. It may be a satisfying dissection with clear margins or a difficult procedure with positive margins on nerve roots and considerable residual disability because of loss of nerve supply to anal and urethral sphincters. The tumors that involve the sacrum above the inferior border of the sacroiliac joints may require dissection or sacrifice of the S3, S2, or even S1 nerve roots. Tumors with an anterior component are approached through a combined abdominolateral approach in a lateral position or sequential abdominosacral positions. Tumors with a large posterior component are approached with the patient in a prone position. Tumors may require en-bloc resection of the rectum or anal canal plus rectum. Following division of the origin of the gluteus maximus muscle from the sacral edge, the pudendal nerve must be spared, because it courses posterior to the ischial spine and then on the surface of the obturator internus in the ischiorectal fossa. The dural sac ends at the S2–3 junction. If the dura is entered, it must be meticulously repaired to prevent a CSF leak. The fused sacral laminae are transected proximally with fine rongeurs. Sacral nerve roots are displaced laterally and the dura superiorly. The fused sacral bodies anteriorly may be divided with an osteotome. Closure is over generous closed-suction drainage.

INTRODUCTION

Sacral tumors may present a difficult problem to the surgeon who desires to obtain a clear margin of excision. Frequently, tumors in this anatomic location are of low grade biologically and therefore unlikely to result in metastatic disease; yet they may be locally persistent. The problem of local control may be made worse by tumor spill resulting from biopsy or incomplete excision by an inexperienced surgeon. Often it may be wise to remove a sacral tumor mass intact without previous biopsy in order to prevent tumor spillage into the resection site, particularly if the resection is not considered likely to result in denervation of the sphincters (Figure 27.1).

INDICATIONS

Resections of the sacrum have been performed for several medical conditions. A limited resection of the distal sacrum (S4 and S5 vertebrae) along with the coccyx has been used in providing exposure, through a posterior approach, of the distal rectum for resection of a villous adenoma or a low anterior resection. In the latter situation, a combined abdominosacral approach

may be used. With the patient in the right lateral position the abdomen is opened and resection of the appropriate portion of sigmoid and rectum performed. Simultaneously, through a transverse incision over the lower sacrum, the distal portion of this bone and the coccyx are removed, providing the necessary exposure for a very low anastomosis.¹ For extensive local recurrence involving the sacrum for colorectal carcinoma, a supine position has been advocated for an anterior transabdominal dissection initially, followed by placement of the patient in a prone position² or a lateral position with the left side down³ for completion of dissection and removal of the sacrum. This plan, although it requires repositioning of the patient and does not permit the guidance in posterior dissection afforded by a simultaneously open abdominal incision, may be the preferable one if extensive, difficult dissection is anticipated anteriorly.

A primary tumor often involving the sacrum is chordoma.^{4,5} Secondary involvement of the sacrum by direct spread is often due to a locally recurrent carcinoma of the rectum.^{6,7}

Meticulous bowel preparation is advisable preoperatively along with perioperative antibiotics. The technique of resection is outlined in the figures below.

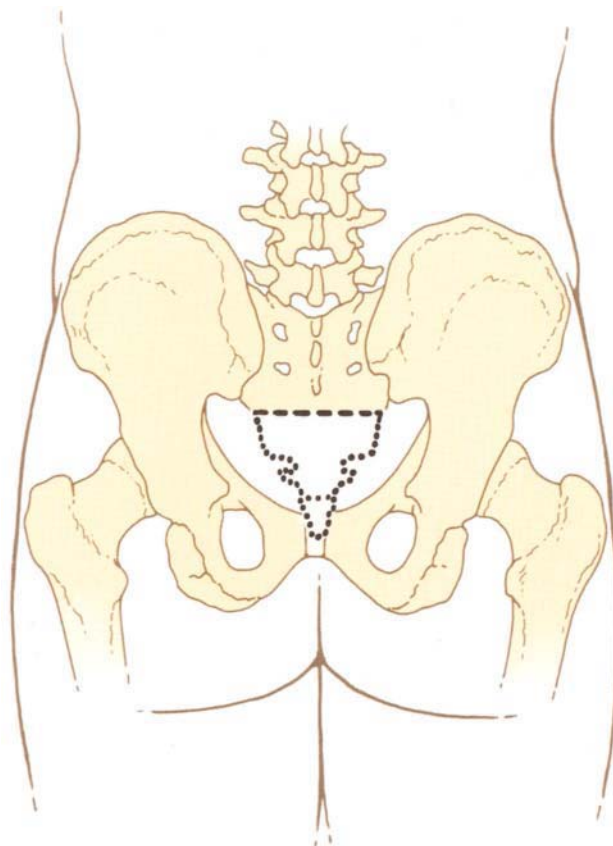


Figure 27.1 The sacrum and the attached tumor mass are removed at the level of the S2–S3 nerve root. The osteotomy is usually just below the sacroiliac joints.

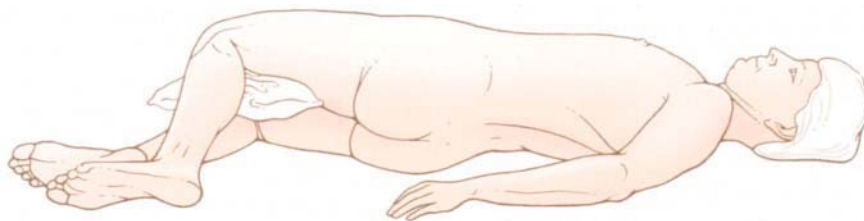


Figure 27.2 Combined abdominolateral sacral position. A combined abdominolateral sacral position is preferred when it is known, or highly suspected, that the rectum is involved, or when previous surgery in this area is expected to have caused dense adhesions between the rectum and the anterior surface of the sacrum. In most of these cases the patient is placed in a lateral position with the left side up, because this makes the mobilization of the rectosigmoid easier. The anterior wall of the abdomen, the left flank, and the sacral area are prepped and draped-in as one continuous field, leaving the iliac crest exposed. The drapes are fixed to the desired position after their placement with skin clips. Posteriorly the entire sacrum is exposed, including the tip of the coccyx, while anteriorly the midline is exposed from above the umbilicus to the pubic symphysis.

If, on the basis of the rectal and/or endoscopic examination, it is known that the rectum is involved, it is usually wise to start with the abdominal portion of the operation. As an abdominal incision one may use an oblique incision extending from the left costal margin to the pubic symphysis, a left paramedian, or a midline can easily be done with some rotation of the table. Not only is the opening and closure more rapid, but also it does not interfere with the construction of the end sigmoid colostomy, which is often needed.

Following disease into the peritoneal cavity, abdominal exploration is carried out to rule out the presence of metastatic disease.

The "white" lines are then incised along the descending and sigmoid colon in order to allow their mobilization. The left ureter is identified and traced down to its insertion to the bladder. The incision in the peritoneum is continued in the retrovesicle or retrouterine area and then to the right of the rectosigmoid. Careful blunt and sharp dissection is now carried out in the presacral space, separating only that portion of rectosigmoid from the upper sacrum that can now be dissected off with minimal effort. Obviously, one should be careful to avoid entering into the tumor as the bowel is separated off the anterior sacral surface. On the other hand it is important, when possible, to free the anterior surface of the first two sacral vertebrae, since their complete resection involves considerable difficulty. The lateral aspects of the rectum are dissected free further down, and the anterior surface is exposed by separating it from the bladder or uterus and upper vagina, to the extent possible through the abdominal approach.

As soon as the decision is made that the rectosigmoid should be resected en-bloc with the sacrum, the bowel mesentery must be divided at the appropriate level. As is true generally of any bowel resection, the peritoneum should be incised first in a radial fashion on either side of the mesentery at the desired level. The adipose tissue is also incised, and the mesenteric arterial and venous branches are exposed. It then becomes obvious how these branches should be divided so that pulsatile blood flow will be present at the end colostomy. The bowel itself is then divided at the midsigmoid portion or distal descending colon as indicated. The distal end is dropped into the pelvis while the proximal end is brought out as an end colostomy.

It is best not to close the abdominal incision at this point lest further dissection be required transabdominally as the sacral resection proceeds. Careful technique should be used to avoid contamination of the incision. The incision over the sacrum is now performed. Flaps, consisting of skin and subcutaneous fat, are developed to the sacral margin, the fibers of the gluteus maximus are divided along the sacral edge, and then the sacrotuberous and sacrospinous ligaments are divided. Following division of the anococcygeal raphe, gentle, blunt finger dissection is performed for a short distance on the anterior surface of the bowel until the level of the transabdominal dissection is reached. Occasionally, in completing the dissection and providing guidance for its safe performance, the simultaneous presence of an operator on the abdominal side is very helpful.

When no part of the rectum can be saved, and an abdominal perineal resection en-bloc with the resection of the sacrum has to be performed, the midline incision over the sacrum is extended inferiorly around and at an appropriate distance from the anal verge. The plane anteriorly between the lower rectum and the prostate or vagina is developed and continued on the sides of the rectum until the level of transabdominal dissection is reached. In this situation no attempt is made to expose the lower anterior surface of the sacrum.

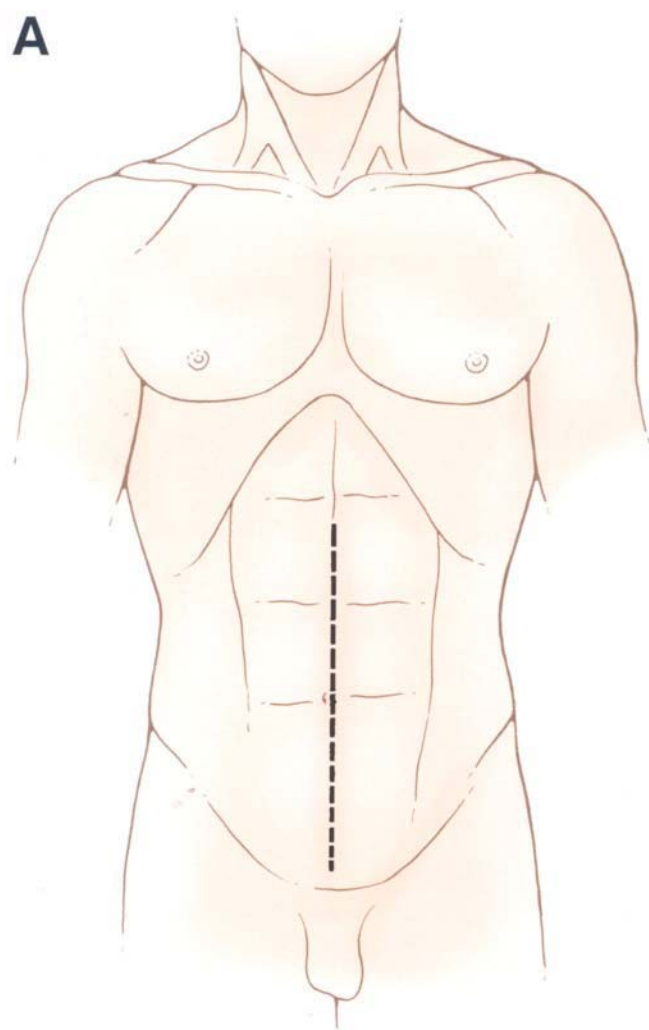
DISCUSSION

Resections of the sacrum are not commonly performed, except in referral centers dealing with these problems. However, given a thorough knowledge of the anatomy of this area and a full knowledge of the principles of dissection, the operation can be performed safely and deliberately. Resections below the body of S3 vertebra do not endanger continence of the anal and bladder functions. Divisions of the bone immediately below or through S2 vertebra or occasionally through S1 are

possible and can be done more safely in terms of avoiding nerve root injury or entrance into the subarachnoid space by cutting first through the posterior sacral plate (the fused sacral laminae) with rongeurs. The sacral canal is thus entered, permitting in some patients the identification, dissection, and preservation of nerve roots that are not involved by the tumor (Figure 27.12).

In two of our patients with high transection of the sacrum the dural sac was entered. In the first, as the bone was divided with an osteotome, a large amount of CSF appeared in the wound, the dural sac was sutured after removal of the specimen, and the wound healed without complications, although the patient had sphincter incontinence. She was required to self-catheterize her bladder three or four times daily and, due to collection of feces in the ampulla, she required frequent disimpaction. In the second patient, with chondrosarcoma reaching the level of S1, the tumor was curetted at that level and treated with intraoperative radiation, but no evident CSF leak occurred intraoperatively. However, postoperatively he developed large collections of CSF in the wound, thus requiring repeat aspirations, and developed meningitis, which required several weeks of antibiotic therapy before it resolved.

Tumors extending into S1 vertebra present a special problem. These have been managed by transecting the bone through the middle of S1. After opening the posterior sacral plate, one carefully dissects laterally whatever nerve roots can be preserved. Residual tumor



B

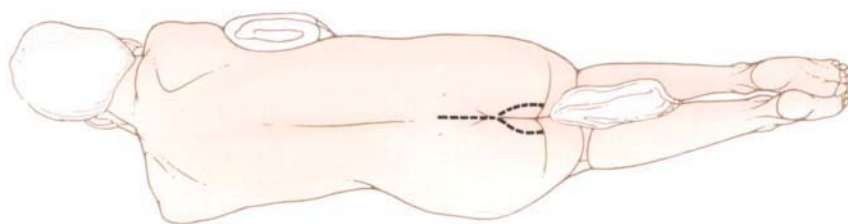


Figure 27.3 Sequential abdominolateral sacral position. Infrequently, wide abdominal dissection may be needed to completely mobilize the intra-abdominal portion of the specimen. If there is extensive visceral tumor involvement or pelvic adhesions, a full midline abdominal incision in a supine position is required. (A) After all attachments to the sacral tumor specimen have been divided, the specimen is usually packed into the pelvis and the abdomen is closed. The patient is turned to a full lateral position. (B) Usually the left side is up, but this may be revised depending on the soft tissue component of the tumor lateral to the sacrum. Visualization is best on the superior margin of the sacrum as the patient is placed in a lateral position.

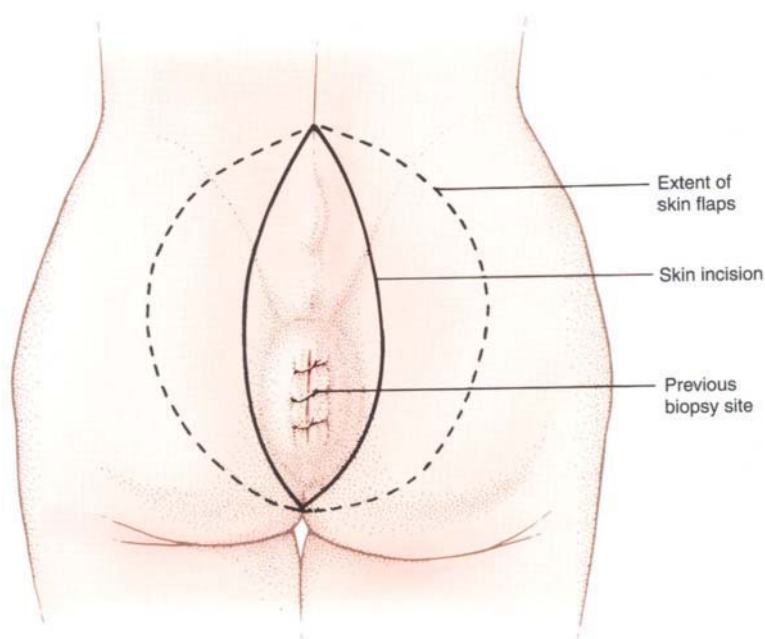


Figure 27.4 Prone position. The prone position is utilized when the tumor mass remains posterior to the rectum and excision of the latter is not required to achieve a tumor-free margin of excision. In the case of a primary tumor of the sacrum, such as a chordoma, when, on rectal and endoscopic examination as well as radiologic evaluation by CT scan, it appears that the rectum is not involved and no prior surgery has been performed that would obliterate the plane between the rectum and the sacrum, it is best to start with the posterior approach. In a substantial portion of patients this will suffice to complete the resection. If the tumor extends into the buttock(s) to a large extent, or is recurrent with multiple deposits, wide exposure of the posterior surface may be needed, and then it is also best to place the patient in a prone position.

A longitudinal incision is performed through the midline. The two ends may curve leftward off the midline or toward the buttock with maximal involvement by tumor. In the presence of a previous biopsy an elliptical incision is made. Curving the two ends of the incision provides greater length and exposure and makes initial development of the flaps easier, especially if tumor extends into the buttock, since the skin in the midline is tethered to the underlying fascia with dense fibrous tissue

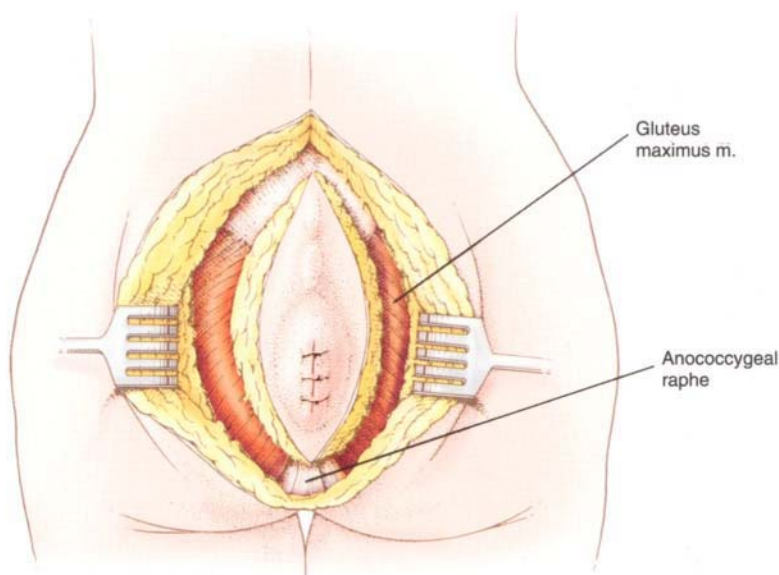


Figure 27.5 Construction of skin flaps. The incision is carried down to the deep fascia and then flaps are raised to the palpable edges of the sacrum or beyond the soft tissue extent of the tumor. The incision stops distally just below the coccyx when it is known that the distal 4–5 cm of the rectum is uninvolved.

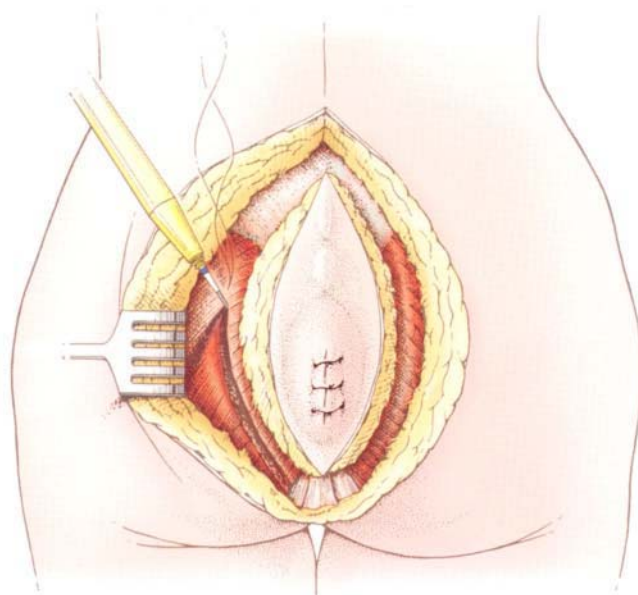


Figure 27.6 Division of gluteus maximus muscles with sparing of sciatic and pudendal nerves. The fibers of the gluteus maximus muscles are divided near their origin from the posterior sacral surface. In the case of a tumor extending beyond the limits of the bone, obviously the dissection is guided by the palpable extent of the tumor.

For large tumors it becomes necessary for a safe resection to expose the sciatic nerves bilaterally, immediately distal to the greater sciatic notch. For such tumors it is also advisable to expose the pudendal nerve, at least one on each side, in the ischiorectal fossa. The anatomic landmark for its identification is the ischial tuberosity. This is easily palpable and is exposed following division of the fibers of gluteus maximus coursing over this bony prominence. The sacrotuberous ligament is divided just medial to the tuberosity, exposing the ischiorectal fossa. The pudendal nerve is found on the lateral wall of this fossa on the surface of the obturator internus muscle. This nerve can be traced proximally as it courses posterior to the sacrospinous ligament, and should be retracted laterally as the latter is divided.

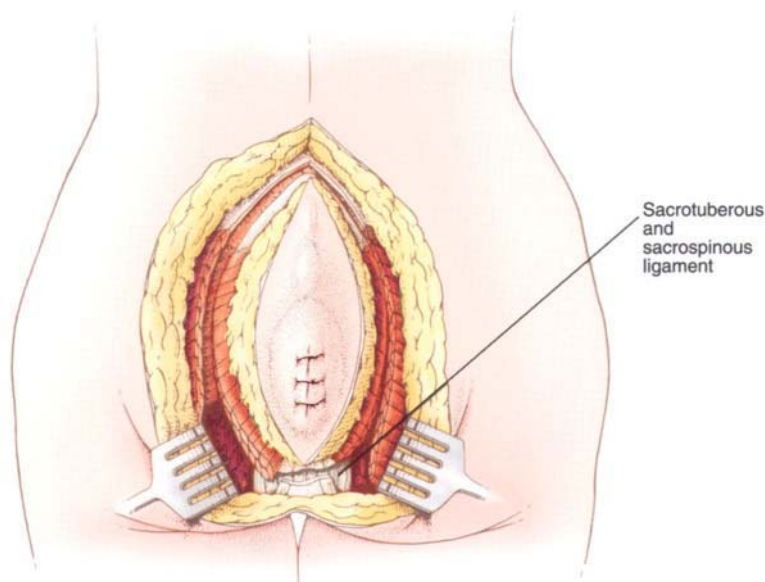


Figure 27.7 Division of the anococcygeal raphe, sacrotuberous, and sacrospinous ligaments. Division of the anococcygeal raphe allows one to enter the presacral space. The dissection along either sacrococcygeal edge is carried out as guided by palpation of the tumor from within the rectum.

After division of the fibers of the gluteus maximus, the thick fibrous bands that constitute the sacrotuberous and sacrospinous ligaments can be palpated. These are divided in order to gain free access to the ischiorectal fossa. On the anterior surface of the sacrum, blunt finger dissection is used to separate sacrum from the posterior rectum.

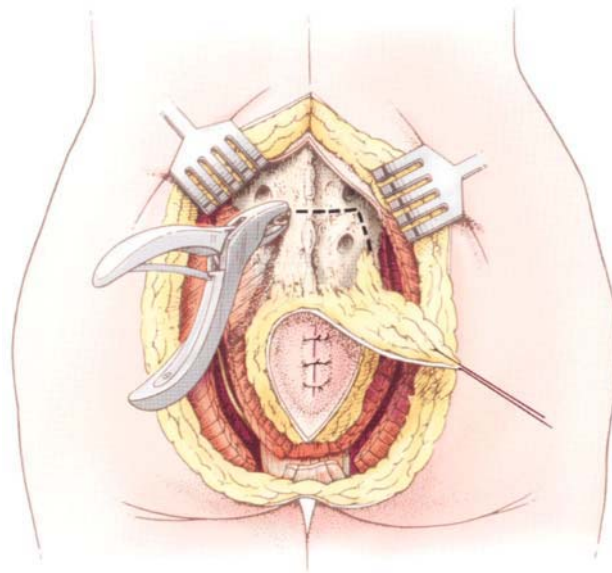


Figure 27.8 Transaction of the sacrum. So far the description has covered the dissection around the lower sacrum with preservation of the rectum. What remains is the dissection through the proximal portion of the bone to complete the resection. It is easier to identify and count the sacral foramina on the anterior surface when the latter is not obscured by tumor. On the basis of the preoperative radiologic studies one should know the level at which the sacrum should be transected. The level of division of the sacrum is of critical importance. Division of this bone just below the lower border of S3 vertebra is safe in preserving sphincteric function. Bilateral sacrifice of S2–S4 nerve roots leads to urinary and fecal incontinence, and impotence for males.^{8–10} Patients about to undergo high sacral resections should be apprised of this risk, because the need for a clear margin of resection is obvious. The tumor, if not operated, is bound to interfere with these functions and pain and further dissemination of the tumor will occur. Unilateral preservation of S2 root maintains perfect anorectal continence, whereas some authors maintain that when both S2 roots are preserved, sphincter problems are mild and reversible.¹¹ Apparently early rehabilitative treatment for 1 year after surgery may restore normal bladder function.¹²

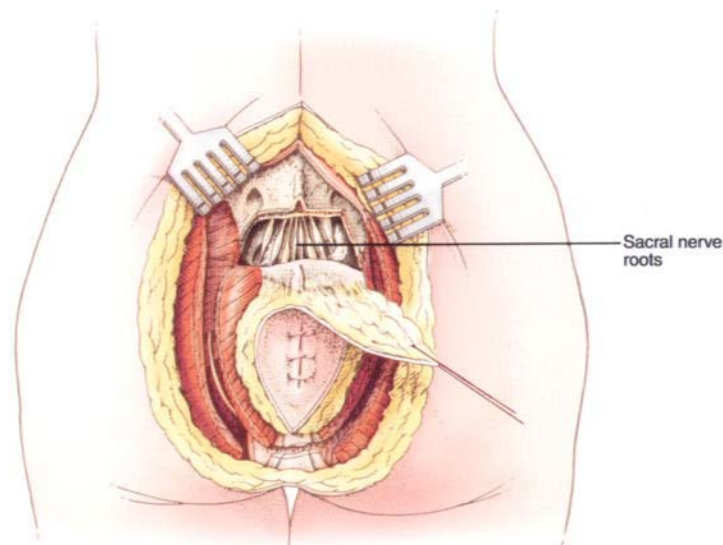


Figure 27.9 Transection of proximal sacrum. If one is able to divide the bone in a straight line, e.g. with a Gigli saw, then one is well below the lower border of S2 vertebrae and generally below the S3 vertebra. The sacroiliac articulation does not allow dissection on the lateral surface of the sacrum, above S3, unless one uses bone instruments. In order to divide the sacrum through S2 or S1 vertebrae, one has to reach at this level along either lateral side by using bone-cutting instruments and then divide the bone across the midline.

In the past it was taught that division of the sacrum proximally should be carried out with an osteotome. However, this technique does not allow any discrimination of what one is dividing. Often it is a matter of 1–2 mm distance between this plane of division and proximal roots of the pudendal nerve. Furthermore, the distance between this plane reaches the level of S2 vertebra and may be entered when the bone is divided with an osteotome. The result can be a disturbing leakage of CSF fluid in the wound, despite suturing of the dura, and potential infection resulting in meningitis.

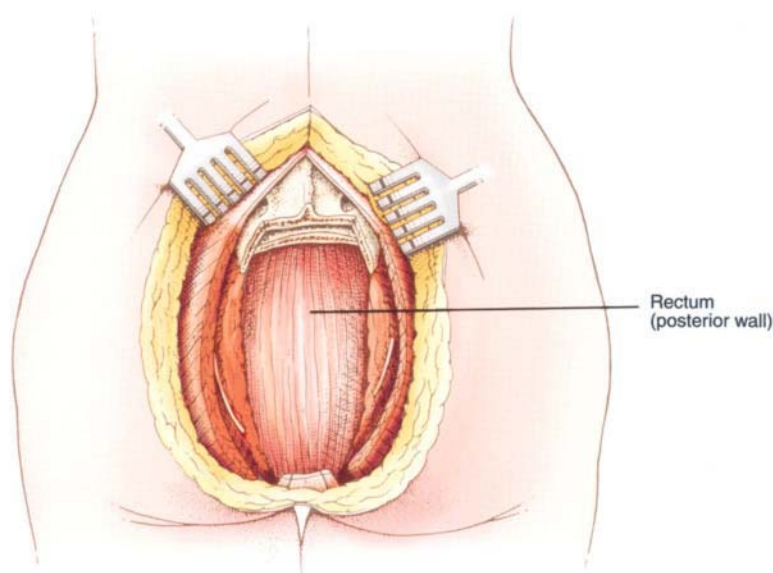


Figure 27.10 Dissecting sacral nerve roots at resection site. A discriminating technique in dividing this bone proximally is the use of fine rongeurs with which the posterior sacral plate is divided at the desired level, and the sacral canal is entered. Nerve roots can then be displaced laterally and the dura superiorly. If one has dissected the pudendal nerve outside the sacrum, one can actually trace its continuity to the S2 root, although the lower roots S3 and S4 may have to be sacrificed. The lower sacral roots may be seen as slender branches issuing from the tumor surface and entering the pudendal nerve. It might thus be possible, if the tumor permits, to salvage the S2 and possibly the S3 roots, unilaterally at least, and their continuation into the pudendal nerve. After the nerve roots have been isolated and preserved, one may then use an osteotome to divide the fused sacral bodies, anteriorly, at this level.

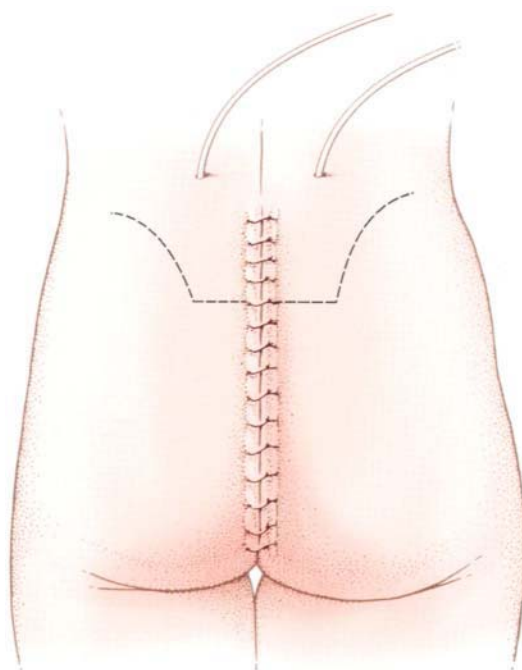


Figure 27.11 Closure. Following removal of the specimen, examination by the pathologist is requested. A frozen section may not be possible if the lesion is confined in the bone, but smears could be obtained from the proximal margins. For interosseous lesions clearly visible on preoperative films, some authors recommend a plain radiograph of the specimen before the incision is closed, in order to assess the margin of resection. The wound is then irrigated and a closed-system drainage with suction is used. The incision is closed in a routine fashion. These wounds have a high rate of wound infection, apparently due to the proximity to the anus.

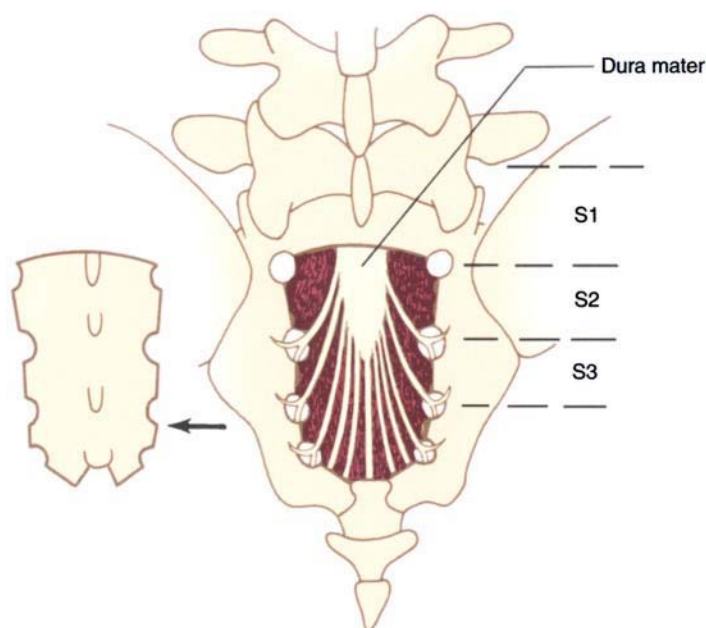


Figure 27.12 Sacral nerve root distribution.

into the proximal half of S1 can be curetted out, and the area of potential microscopic residuum treated later with radiation. A dose of intraoperative radiation may also be given, when available, with the pelvic viscera appropriately shielded. The preliminary evidence from other centers also suggests that this may be helpful.¹³

Complete resection of the sacrum is seldom, if ever, practiced. There is a concern first for the removal of support for the spinal column that the sacrum provides. Experience, with hemisacrectomies, entailing division below the body of L5, however, suggests that removal of the entire sacrum would not be likely to result in "collapse" of the spine, or some other catastrophic occurrence. However, the sciatic nerve comprises L4 through S3 nerve roots. The lumbosacral trunk (L4, L5) courses over the sacral ala, and S1, S2, and S3 roots issue through the upper three anterior sacral foramina.

It is therefore clear that a radical resection of the entire sacrum would result, in addition to sphincteric incontinence, in considerable denervation of both lower extremities in the distribution of the sciatic nerves.

As in other anatomic areas, the cure rate following sacral resection depends on the adequacy of resection, the use of adjuvant modalities, and the biologic nature of the tumor. Local spill of tumor cells with biopsy, or partial resection by an inexperienced surgeon, may severely compromise the opportunity for a complete recovery.^{14,15} This is very clear from experience with chordoma excision. For localized tumors, resections of the sacrum, when involved, can be performed safely if certain oncologic principles are followed. Often there is preservation of sphincteric control, and the result is cure or significant palliation.

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Periacetabular Resections

Martin Malawer

OVERVIEW

The traditional treatment of periacetabular sarcomas has been a classical hemipelvectomy; that is, an amputation through the sacroiliac joint and symphysis pubis. Limb-sparing surgery, i.e. periacetabular resection and reconstruction, has been notoriously difficult. Tumors of the periacetabular area are difficult to treat and traditionally have a high complication and morbidity rate. The surgical alternatives for reconstruction of a periacetabular defect have been iliofemoral arthrodesis, ischiofemoral arthrodesis, or flail extremity. Within the past decade the development of a saddle prosthesis by Waldemar-Link (Hamburg, Germany) has made the reconstruction of periacetabular defects more satisfactory and has dramatically decreased surgical morbidity.

The surgical anatomy of the pelvis must be well understood in order to perform a periacetabular resection safely. The key to success is wide exposure both anteriorly, i.e., retroperitoneal (ilioinguinal incision) and posteriorly, a large gluteus maximus fasciocutaneous flap to expose the retrogluteal area. The retrogluteal area consists of the ilium, sciatic notch, sciatic nerve, and hip joint. This combined exposure permits safe dissection of large tumors of the acetabulum and preservation of the important neurovascular and visceral structures. Reconstruction can easily be performed through this approach.

Imaging studies are extremely important in order to determine the extent of the tumor within the periacetabular region of the pelvis. The tumor must be confined to the lower portion of the ilium and the periacetabulum but may extend into the pubic rami. Specifically, a combination Type II and III pelvic resection can be performed versus a pure Type II, periacetabular resection. CT, MRI, and bone scan is required to determine the level of iliac resection as well as the sites of the other osteotomies.

Angiography is required to determine iliac vessel displacement, especially the hypogastric (internal iliac) artery, and venography is utilized to determine the presence of intramural tumor thrombi. The hypogastric artery is usually ligated. CT scan, in conjunction with MRI, is useful to determine the extraosseous component and the extension into the pelvis as well as the retrogluteal area.

The utilitarian incision of the pelvis is used to expose the retroperitoneal area to mobilize the iliac vessels and to mobilize the tumor. The superior pubic ramus is identified anteriorly by retraction of the iliac femoral vessels. Posteriorly, the sciatic notch in the ilium is identified and an osteotomy is performed through the sciatic notch with the sciatic nerve protected. The third osteotomy is through the ischium or the posterior column, depending on the exact location of the tumor. The entire periacetabular tumor can then be removed posteriorly after detaching the sacrospinous ligament.

Several different methods of reconstruction have been developed over the past two decades: ischiofemoral arthrodesis, pelvic allograft, iliofemoral arthrodesis, and a flail hip; however, this chapter will emphasize the use of the saddle prosthesis. The chapter will discuss the use of the saddle prosthesis, its unique surgical and technical considerations (especially of a notchplasty) and the muscle reconstruction required in order to obtain a good functional result.

INTRODUCTION

Five percent of primary malignant bone tumors involve the pelvis. Osteosarcoma in adolescents, Ewing's sarcoma in children, and chondrosarcoma in adults are the most common primary sarcomas in this location. More commonly, though, neoplasms involving the pelvis occur as a result of metastatic spread from the breast, lung, prostate, kidney, or thyroid. Diffuse involvement of the pelvis is often seen, but bony destruction of the periacetabulum is of greatest concern as patients often present with severe pain and dysfunction that may not respond to limited weight-bearing and radiotherapy alone.

Tumors arising in the periacetabular region of the pelvis pose a difficult problem (Figure 28.1). Classically, hemipelvectomy was the primary means of surgical intervention. With the advent of aggressive chemotherapy, better imaging studies and more advanced surgical techniques, limb-sparing resections have been carried out for primary malignancies of the pelvis and metastatic lesions that have failed other forms of treatment. Periacetabular resections should accomplish the goal of achieving an adequate tumor resection with minimal morbidity followed by a reliable and functional reconstruction. Techniques of surgical reconstruction include: ischiofemoral arthrodesis, iliofemoral arthrodesis, pelvic allograft, custom prosthesis, flail extremity, and, more recently, a custom saddle prosthesis.

Given the complexity of the anatomy and the use of adjuvant therapies that require an uncomplicated and expedient postoperative recovery, osseous pelvic resections remain one of the greatest surgical challenges. This chapter will discuss the senior author's experience with saddle prostheses as a means of safe, reliable, pelvic reconstruction.

UNIQUE ANATOMIC CONSIDERATIONS

Pelvic Muscles

The pelvis is virtually covered by muscle that acts as a barrier to tumor extension into adjacent vessels and nerves. This is especially true of tumors arising in the ilium and periacetabular region.

1. *Iliacus*. This muscle provides protection from tumors extending from the inner cortex of the ilium. It often contains the tumor until it becomes very large, and usually provides an adequate margin of resection.
2. *Gluteus medius and minimus*. These muscles cover the superior and inferior aspects of the outer cortex of the ilium.
3. *Piriformis*. This muscle, which extends from the sacrum to the greater trochanter, fills the greater

sciatic notch and tends to protect the sciatic nerve from tumors that extend in this area.

Neurovascular Bundle

1. *Femoral vessels and nerve*. Tumors arising from the superior pubic ramus are close to these structures (see Figure 28.1). A thick neurovascular sheath usually protects them from tumor extension. If necessary, the femoral vessels and nerve can be carefully dissected free from the sheath, leaving it with the resected specimen.
2. *Sciatic nerve*. Tumors extending from the ilium into the sciatic notch may be immediately adjacent to this nerve. Usually the nerve is not directly infiltrated and can be dissected free from the tumor pseudocapsule.

Bladder/Urethra

The bladder is separated from the anterior pubis by thick fibrous tissue that is an extension of the pecten pubis and the retropubic fat. The urethra, located just inferior to the symphysis pubis, is separated from it by the arcuate ligament. The surgeon must protect these structures when dealing with tumors arising from the anterior pelvis.

Sacroiliac Joint

Extension of tumor across the joints of the pelvis is frequently reported. Careful preoperative and intraoperative evaluation of the sacroiliac joint is necessary (Figure 28.2). Pelvic tumor extension, in particular chondrosarcoma, can be difficult to evaluate even with modern imaging modalities.

Pelvic Veins

Tumor thrombi within the large pelvic veins have been reported for pelvic sarcomas. Meticulous preoperative evaluation with the use of MRI and venography is necessary.

IMAGING STUDIES

Appropriate imaging studies are the key to successful resection of tumors of the pelvis and acetabulum. Computed tomography (CT), magnetic resonance imaging (MRI), angiography, and bone scintigraphy (three-phase bone scan) are the most useful preoperative studies. For tumors of the pelvis and acetabulum with a large extraosseous component, a venogram may be warranted if there is evidence of distal obstruction.

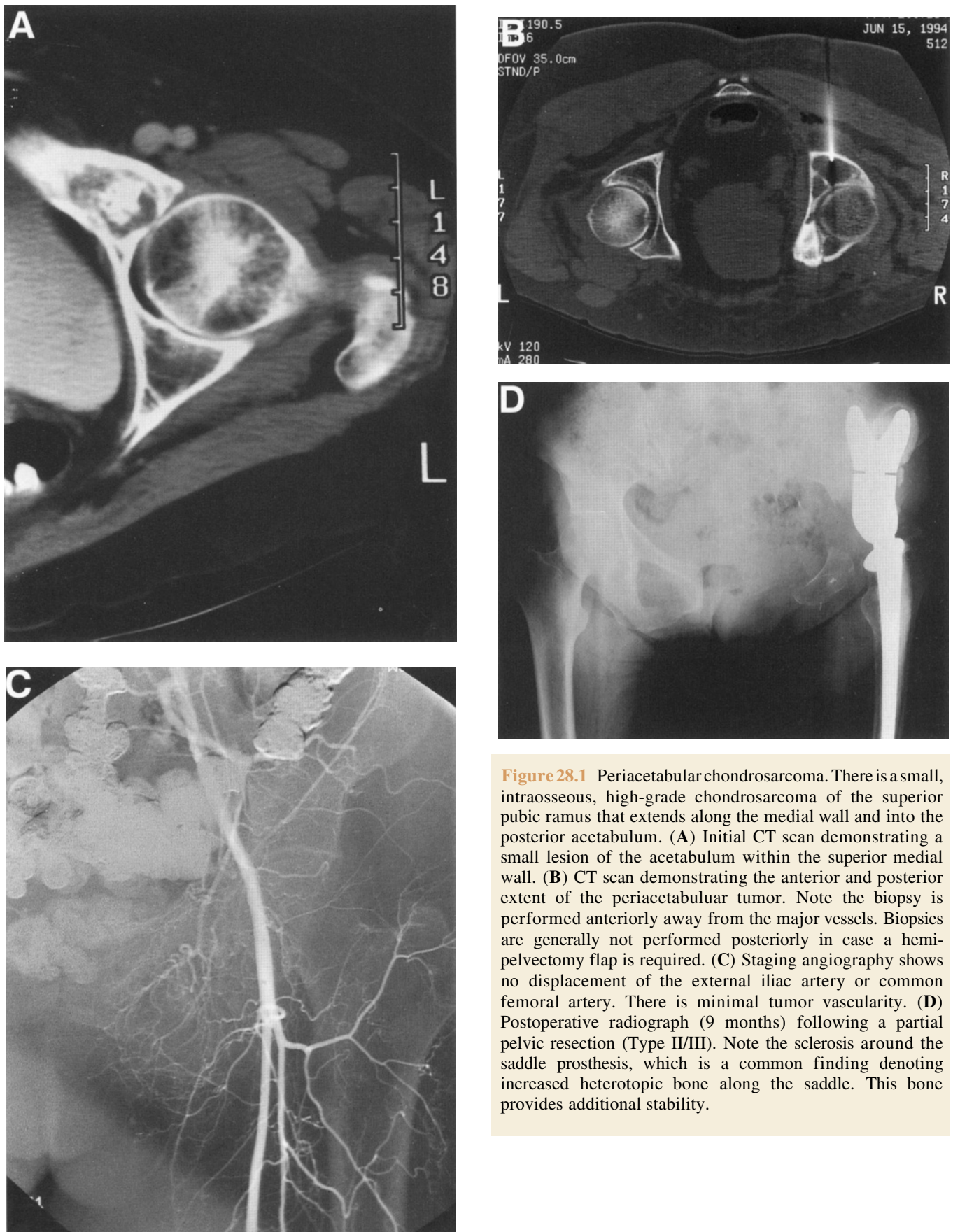


Figure 28.1 Periacetabular chondrosarcoma. There is a small, intraosseous, high-grade chondrosarcoma of the superior pubic ramus that extends along the medial wall and into the posterior acetabulum. (A) Initial CT scan demonstrating a small lesion of the acetabulum within the superior medial wall. (B) CT scan demonstrating the anterior and posterior extent of the periacetabular tumor. Note the biopsy is performed anteriorly away from the major vessels. Biopsies are generally not performed posteriorly in case a hemipelvectomy flap is required. (C) Staging angiography shows no displacement of the external iliac artery or common femoral artery. There is minimal tumor vascularity. (D) Postoperative radiograph (9 months) following a partial pelvic resection (Type II/III). Note the sclerosis around the saddle prosthesis, which is a common finding denoting increased heterotopic bone along the saddle. This bone provides additional stability.

The information to be obtained from each of these studies is as follows:

Radiographs

The radiographic characterization of most bone lesions on the initial plain films of the pelvis usually gives an indication of whether the tumor is a primary sarcoma, metastatic lesion, or benign process. These findings may be very subtle, however, so that one must be extremely cautious in their interpretation (e.g. chondrosarcoma of



Figure 28.2 A large chondrosarcoma of the ilium involving the adjacent sacral alar. CT scans are extremely useful in determining SI joint and sacral alar involvement. If the sacrum is involved, a limb-sparing resection and even a hemipelvectomy often cannot be performed.

the pelvis). A patient with persistent pain in the hip or pelvic region, despite "normal" plain radiographs, should be further evaluated with additional imaging studies.

Bone Scan

The bone scan is used to assess the extent of tumor involvement and to evaluate for metastases. The flow phase and blood pool images are also helpful in assessing tumor vascularity. Tumor extension into the ilium and pelvic columns must be evaluated.

CT Scan

Because it shows mineralization, CT is superior to MRI for visualizing subtle cortical destruction, calcification or ossification, and fracture (Figure 28.3). This remains the study of choice by many for evaluation of the degree of cortical destruction of the pelvis, which is often critical in the periacetabular region (i.e. in evaluating the acetabular dome and columns of the pelvis). CT provides more reliable imaging for determination of the effects of induction chemotherapy and bone response. It is considered complementary to MRI in evaluating soft-tissue extent and displacement of adjacent nerves and vessels. Careful evaluation of iliac extension is required.

MRI

Magnetic resonance is the imaging method of choice for detecting tumor extension into the hip joint, sacroiliac joint, or sacrum, and extension into the superior

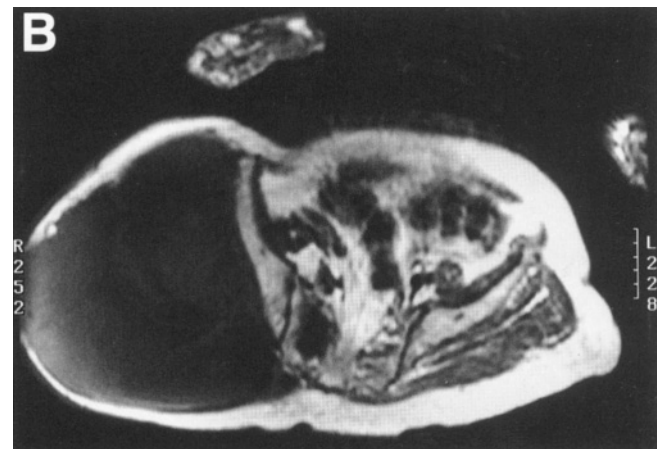
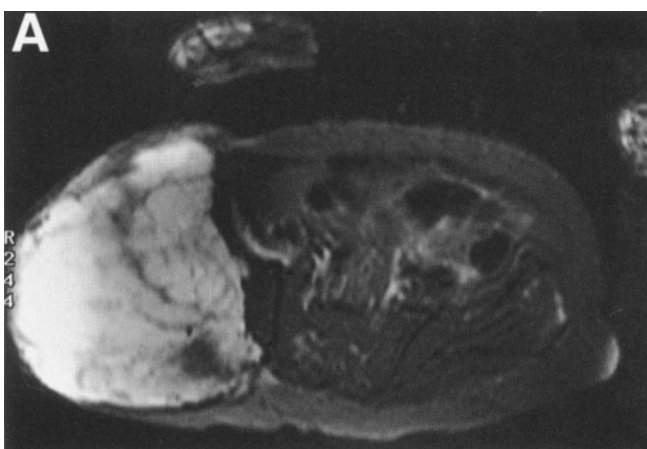


Figure 28.3 MRI scan of an extremely large chondrosarcoma arising from the wing of the ilium and the periacetabular bone. (A) The high-intensity area represents gross tumor permeating through the ilium. Note that there is no intrapelvic extension. (B) The large soft-tissue component is seen arising from the underlying ilium. It involves the sacral alar and the SI joint. This tumor is inoperable.

pubic rami and ischial region (Figure 28.3). MRI shows the fat of the marrow with superior contrast, and is therefore the best modality to demonstrate intraosseous tumor extension. This is extremely important in tumors that demonstrate subtle infiltration within the ilium, such as chondrosarcoma. MRI is superior for evaluation of soft-tissue tumor extent and for evaluating critical neurovascular structures (i.e. sacral plexus and iliac vessels) (Figure 28.4). If tumor extends to the superior pubic ramus or the ischium, then a combined Type II/III resection is required.

Arteriography/Venography

Although MRI and MRA (magnetic resonance arteriography) can be used to visualize the pelvic vessels, arteriography remains the most useful study for evaluating tumor vascularity and anatomy. It more accurately assesses the vascular anatomy, including anatomic variants and anomalies. Arteriography is the most reliable study to determine the response to neoadjuvant chemotherapy. The venous flow phase is useful to detect venous occlusion or tumor thrombi. If there is any suggestion of venous occlusion, a formal venogram should be performed. The femoral vessels are often displaced by large periacetabular tumors.

Biopsy

The biopsy technique and placement is of paramount importance in periacetabular tumors as the risk of peritoneal and pelvic contamination is considerable and local control is a greater challenge (Figure 28.1). A misplaced or poorly performed biopsy can lead to extensive soft-tissue contamination and render resection difficult or not feasible. A poorly performed biopsy may be the primary reason a patient has a hemipelvectomy, and it may even interfere with soft-tissue flaps necessary for wound coverage.

Most patients with periacetabular tumors are best served with a needle biopsy placed in the incision line of the planned future resection. CT guidance should be used unless there is a large extraosseous component that is easily accessible and away from critical neurovascular structures. The needle biopsy is performed anteriorly. The posterior approach should be avoided so as not to contaminate the gluteus maximus, hip joint, femoral vessels, and femoral nerve.

A patient who has a needle biopsy that does not provide a definitive diagnosis should undergo an open incisional biopsy in the operating room, with special emphasis on biopsy placement and ensuring adequate tissue for diagnosis.

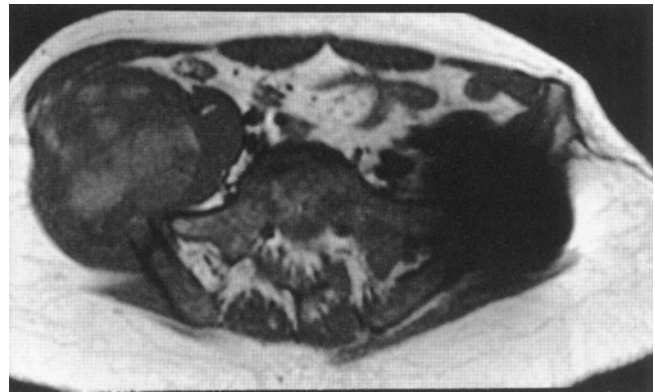


Figure 28.4 MRI scan of a high-grade sarcoma arising from the ilium, crossing the SI joint, and involving the L5 transverse process. This tumor is considered to be unresectable due to the extension along the sacrum and the lumbar spine. MRI scans are invaluable in determining extraosseous soft-tissue extension of bony tumors.

INDICATIONS AND CONTRAINDICATIONS OF LIMB-SPARING SURGERY

Most primary periacetabular tumors can be resected without amputating the lower extremity. Periacetabular resection is indicated in cases in which: (1) surgical margins similar to those obtained with a hemipelvectomy can be accomplished; (2) the resection (and reconstruction) can preserve a reasonably functional limb; (3) the life expectancy and general physical status of the patient justify the procedure. Contraindications include: (1) local recurrence following a previous limb-sparing resection unless the recurrence can be widely resected or the amputation offers no oncologic benefit; (2) tumor extension posteriorly across the sacroiliac joint with involvement of the sacral nerves and nerve root foramen; (3) tumors which extensively infiltrate the soft tissues of the pelvis and extend into the thigh with or without involvement of the sciatic nerve; (4) poor overall physical status or limited life expectancy.

DESCRIPTION OF IMPLANTS

Saddle Prosthesis

The saddle prosthesis was originally designed for reconstruction in patients who sustained extensive loss of acetabular bone after failed total hip arthroplasty. Similar defects are often encountered following periacetabular tumor resection, with previously described reconstruction techniques being fraught with high local morbidity and complication rates. Since 1988 the authors have used the saddle prosthesis, with favorable results, for reconstruction of the pelvis following Type

II and Type II/III periacetabular resections for primary sarcomas and in patients with metastatic disease.

Since its initial development the prosthesis has undergone several design changes to address design-related problems. The unique and crucial surgical considerations for implanting the saddle prosthesis should be emphasized. These include: retaining at least 2 cm of remaining ilium following tumor resection, creating a notch within the remaining ilium that is within the depth of the saddle component and is located in the

thickest (medial) portion of bone, retaining the iliopsoas and abductor muscles and adjusting the pelvic–femoral tension with the correct interpositional base component length (see Surgical Technique, below).

The metal saddle component rests on a polyethylene-bearing sleeve which rotates on a peg attached to the base component (Figure 28.5). The base component is available in several lengths to accommodate variable amounts of bone loss following tumor resection. The base is attached to the stem taper in place of a femoral head.

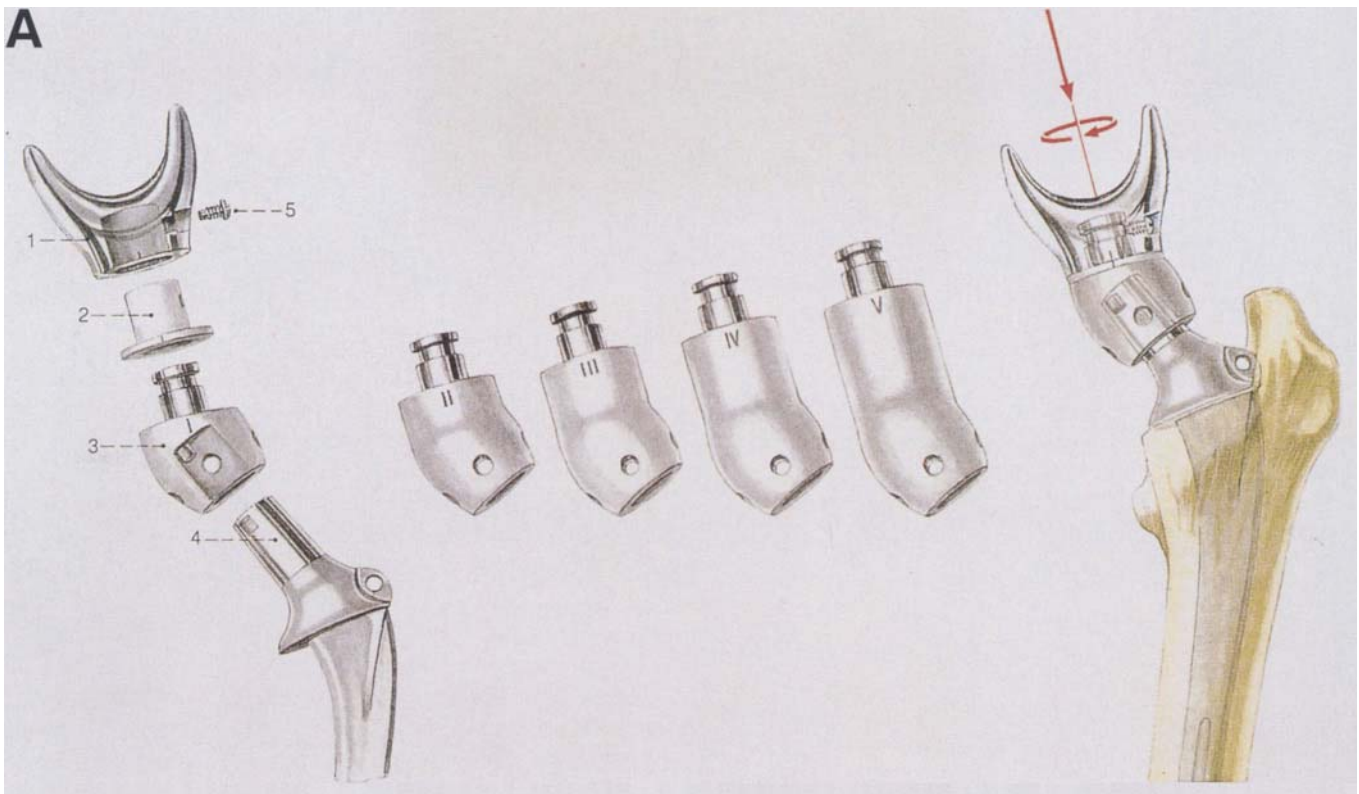


Figure 28.5 (see also following page) (A) Saddle prosthesis for periacetabular replacement and reconstruction. The saddle prosthesis (Waldemar-Link, Hamburg, Germany) was originally developed for use in total hip revision surgery. This prosthesis is now used to reconstruct the pelvis following periacetabular resections. The prosthesis consists of three components: the femoral stem (4), base element (body) (3), and the saddle portion (1) that articulates with the ilium. (B) Degrees of motion of saddle prosthesis. The saddle is free to rotate on the body component. The entire prosthesis can abduct, adduct, flex, and extend through the saddle and iliac "articulation". (C) Periacetabular resection (Type III) with the saddle prosthesis reconstruction. (D) Reconstruction. Photograph of the pelvic bony structure. The lines are demarcating the extent of a periacetabular resection. The superacetabular osteotomy can be performed close to the acetabulum or as high as the sciatic notch (as shown). The lower the osteotomy, the more stable the prosthesis. The osteotomy along the superior pubic ramus can be made along the medial wall up to the symphysis pubis. The osteotomy of the inferior pubic ramus or pubic bone can be performed at several different levels according to the oncological needs. In general, periacetabular reconstructions are performed with a saddle prosthesis (Waldemar-Link, Hamburg, Germany). (E) Type II and Type III combined pelvic resection for a large, high-grade chondrosarcoma reconstructed with a saddle prosthesis. Note the typical reossification which occurs around the pericapsular structure (forms around the saddle component). This reactive bone is typically seen between 12 and 16 months. This reactive bone (arrows) increases the stability of the prosthesis. Adequate reconstruction consists of the preservation of the iliopsoas muscle, the abductor muscles, and the use of a notch within the ilium to create stability for the saddle. (Courtesy of Link America, Danville, NJ). Reprinted with permission from Stuttgart, Germany, Georg Thieme Verlag from Bauer, Kerschbaumer, Poisel: *Orthopedic Operations*, pp. 296–307.

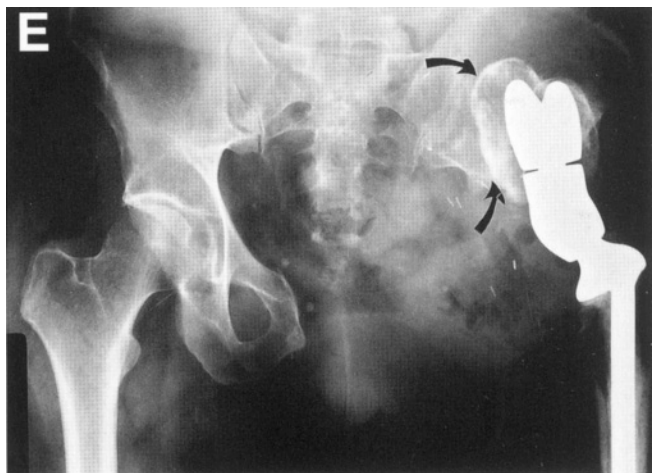
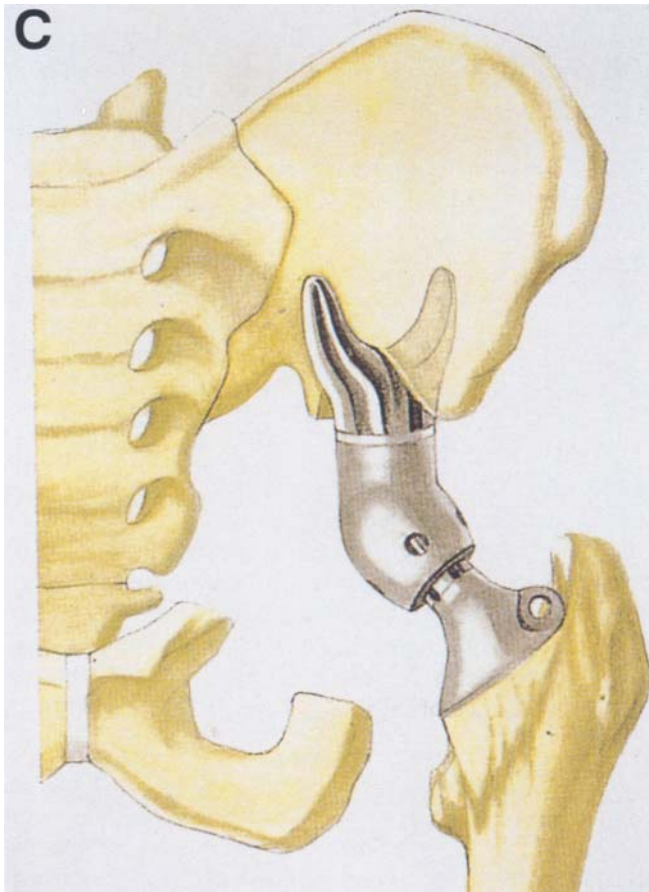
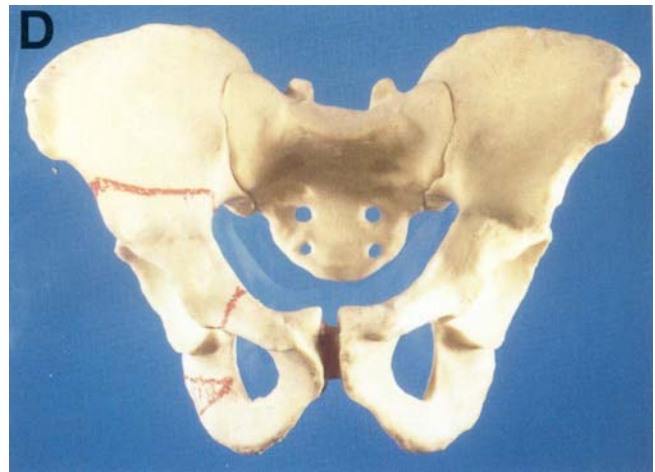
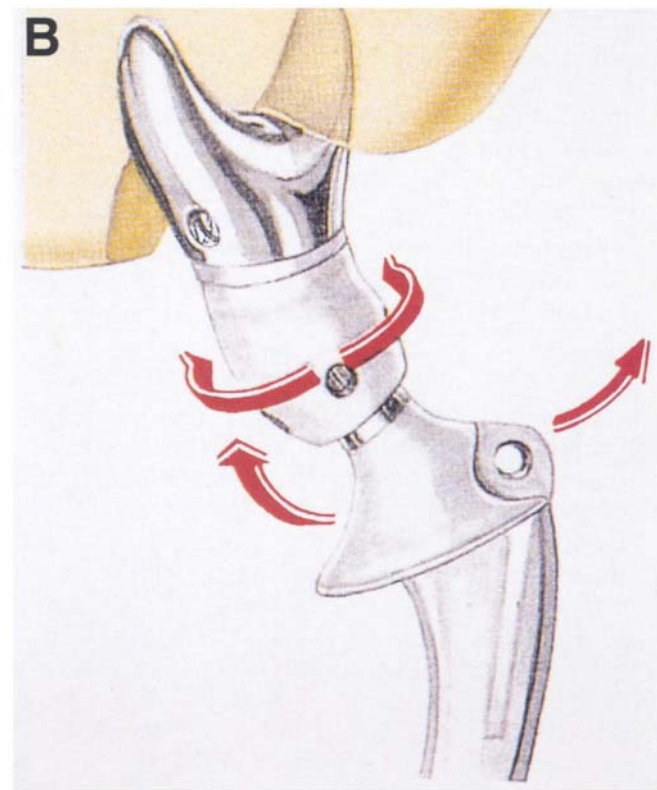


Figure 28.5 B–E

A blunt-tipped set screw engages a circumferential groove in the peg (without placing any load on the metal). The set screw prevents the saddle and base component from dislocating.

A locking pin located within the conical recess of the base engages an eccentric slot in the face of the taper. This prevents rotational instability within the conical mounting. This is necessary because axial forces (depending on the length of the base component) can occur in the saddle prosthesis, unlike an implant with a spherical femoral head.

Anatomy

The saddle component of the prosthesis articulates against a notch that the surgeon makes in the medial portion of the remaining ilium. One horn of the saddle lies within the true pelvis and is covered by the iliopsoas muscle. The other horn of the saddle is located outside the pelvis and is covered by the gluteus medius and minimus muscles.

Motion

The articulation between the saddle and iliac bone permits the leg to be turned in any direction (Figure 28.5C). Rotation is made possible within the articulation between the saddle and the base component.

SURGICAL GUIDELINES

1. The utilitarian incision is utilized to expose both the anterior (internal) and posterior (extrapelvic) aspects of the pelvis. The ilioinguinal incision is utilized to develop the retroperitoneal plane and the posterior gluteus maximus fasciocutaneous flap is utilized to develop the retrogluteal space.
2. The iliac vessels are initially mobilized and the hypogastric artery is identified and may be ligated. The sciatic and femoral nerves are identified and protected.
3. The level of osteotomy through the ilium is identified from within the pelvis as well as the superior pubic rami. Identification of the superior pubic rami requires mobilization of the external iliac and femoral vessels as they cross the ramus.
4. A large posterior myocutaneous flap is developed with the gluteus maximus muscle. The gluteal maximus muscle is detached from the iliotibial band and femur so as to be retracted posteriorly. This exposes the retrogluteal space; the ilium, sciatic notch, sciatic nerve, and hip joint.
5. The ischium is identified through the posterior incision and is osteotomized above the level of the biceps tendon insertion.
6. Complete removal of the periacetabulum requires the release of the sacrospinous ligament and some of the pelvic floor musculature.
7. Reconstruction of the periacetabular defect is performed with the saddle prosthesis (Link®, Hamburg, Germany).

Postoperative immobilization is required for 10–14 days with the lower extremity in abduction to protect the prosthesis and the abductor muscles. A hip abduction brace is utilized for 3 months. Physical therapy and rehabilitation requires 6–9 months to become fully ambulatory with a cane.

RECONSTRUCTION FOLLOWING RESECTION OF PRIMARY PERIACETABULAR TUMORS

Saddle Prosthesis Schematic of Surgical Procedures (Figures 28.6–28.8)

Notchplasty (Figure 28.6)

A notch is created in the remaining ilium using a high-speed burr. The notch should be placed in the thickest

region of the remaining bone (usually medial). The notch accommodates the saddle component of the saddle prosthesis and its depth matches that of the saddle. When positioned intraoperatively the notch between the two horns of the saddle prosthesis is perpendicular to the notch created in the bone. The notch facilitates articulation between the saddle prosthesis and the remaining ilium and lends stability during subsequent hip motion (Figure 28.6).

Preparation of the Proximal Femur

The proximal femur is prepared as for a standard femoral component. The proximal femur intramedullary canal is reamed to accept the largest diameter stem and allow for a 2-mm circumferential cement mantle. Once reaming is completed, and the appropriate-sized stem (diameter and length) is selected, a distal femoral cement plug is inserted to a depth of 2 cm below the tip of the selected femoral stem. The femoral canal is then irrigated with saline and packed with gauze. Once the cement (PMMA) is prepared, the gauze is removed and femoral prosthesis is cemented within the proximal femur.

Trial Reduction (Figure 28.7)

A reduction using trial components is critical in assessing the accurate length of the base component (intercalary segment) and determining optimum soft-tissue tension. The base component length selected should be determined by the distance between the ilium and femoral neck cuts, as the length indicated on the base component is the total length from the notch of the saddle to the femoral collar. A base component should be selected where reduction is barely possible with minimum “play” in the reduced joint. The surgeon should be able to reattach the abductor mechanism to its anatomic position on the osteotomized greater trochanter.

A trial reduction can also determine areas where the saddle component may impinge on the existing notch during intraoperative range of motion. These areas can be further contoured with a high-speed burr to prevent impingement (which may result in limited motion or dislocation). Hip motion (flexion to at least 90 degrees, extension to 30 degrees, abduction to 45 degrees, adduction to neutral, and rotation) should be possible without evidence of impingement or dislocation.

Abductor Mechanism Reconstruction (Figure 28.8)

The osteotomized greater trochanter and abductors are reattached to their original location using cables. If the

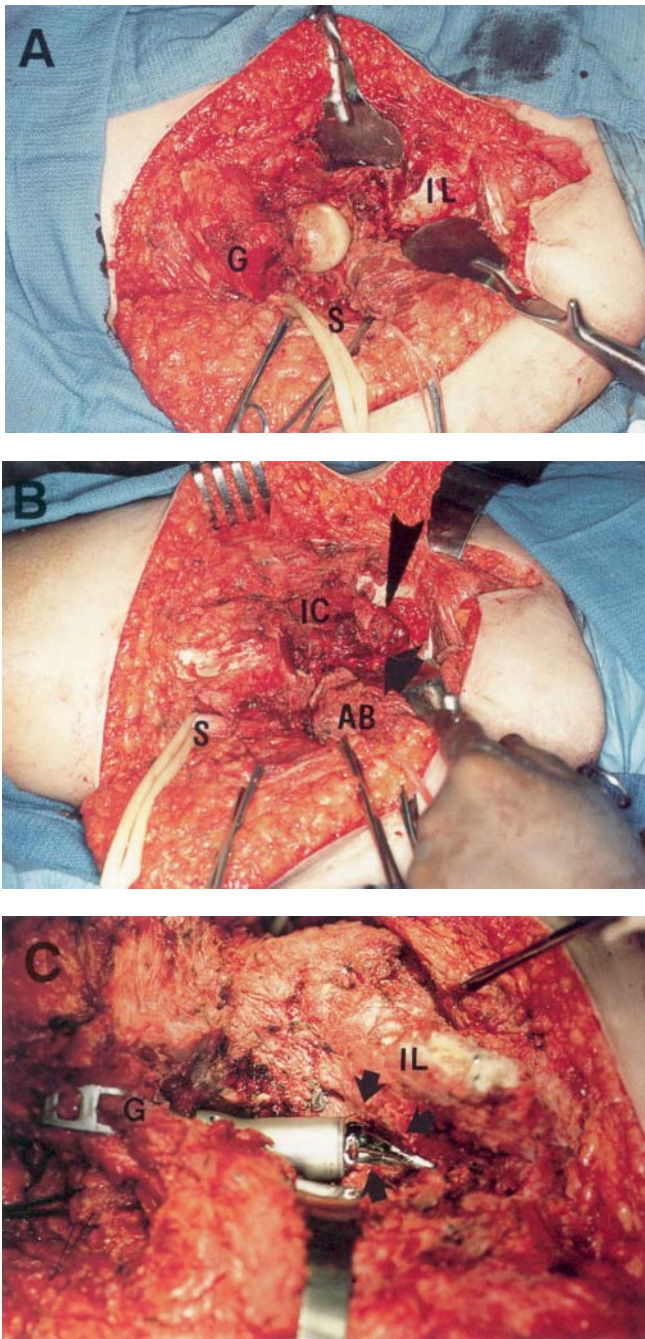


Figure 28.6 (A) Photograph following a periacetabular resection showing the remaining ilium (IL), sciatic nerve (S), the greater trochanteric osteotomy (G), and the femoral head. This defect is reconstructed with a saddle prosthesis. This necessitates removal of the femoral head with the insertion of the femoral component, a base element, and a saddle that articulates with the notch (made by the surgeon) in the ilium. (B) Intraoperative photograph demonstrating the creation of the deep notch (large arrows). The notch gives immediate stability to the prosthesis and permits an articulation between the saddle and the ilium. The saddle is not cemented or otherwise fixed into this notch. The tension of the muscles and the length of the body of the prosthesis creates the tension that is required. The abductors, psoas, and iliacus muscles must be placed under appropriate tension to maintain stability of the prosthesis (AB shows abductor muscles; IC shows the iliacus muscle; S shows the sciatic nerve). (C) Reduction of the saddle prosthesis into the iliac notch (IL). The notch (solid arrows) must be as deep as the saddle and permit approximately 45° of flexion and extension, as well as abduction and adduction. The gluteal muscles (G) have already been opposed to the greater trochanter with a cable grip system. Closure then consists of reattaching the abductors and closing the ilioinguinal incision.

(or prosthesis). The gluteus maximus muscle is then reattached to its insertion using nonabsorbable suture.

Wound Closure

The wound is copiously irrigated with saline. A large chest tube drain is inserted beneath the fascial closure. The subcutaneous tissue is closed over suction drains using absorbable suture. The skin is closed with suture or staples.

Functional and Rehabilitation Considerations

Function

In general, patients who undergo resection and reconstruction for a periacetabular tumor are able to ambulate (with or without a cane) following rehabilitation. It may take up to 1 year to regain motor strength, especially if the hip abductors were reconstructed or a more extensive resection was required (Type II/III).

Rehabilitation

The rehabilitation process is dependent on the extent of tumor resection (bone and soft tissue), the required

greater trochanter was included in the resected specimen the abductor mechanism is reattached to the prosthesis using 3 mm Dacron tapes. Soft-tissue tension and prosthetic stability are again tested once the abductor mechanism reconstruction is complete. The piriformis and short external rotator muscles are brought forward and reattached to the proximal femur

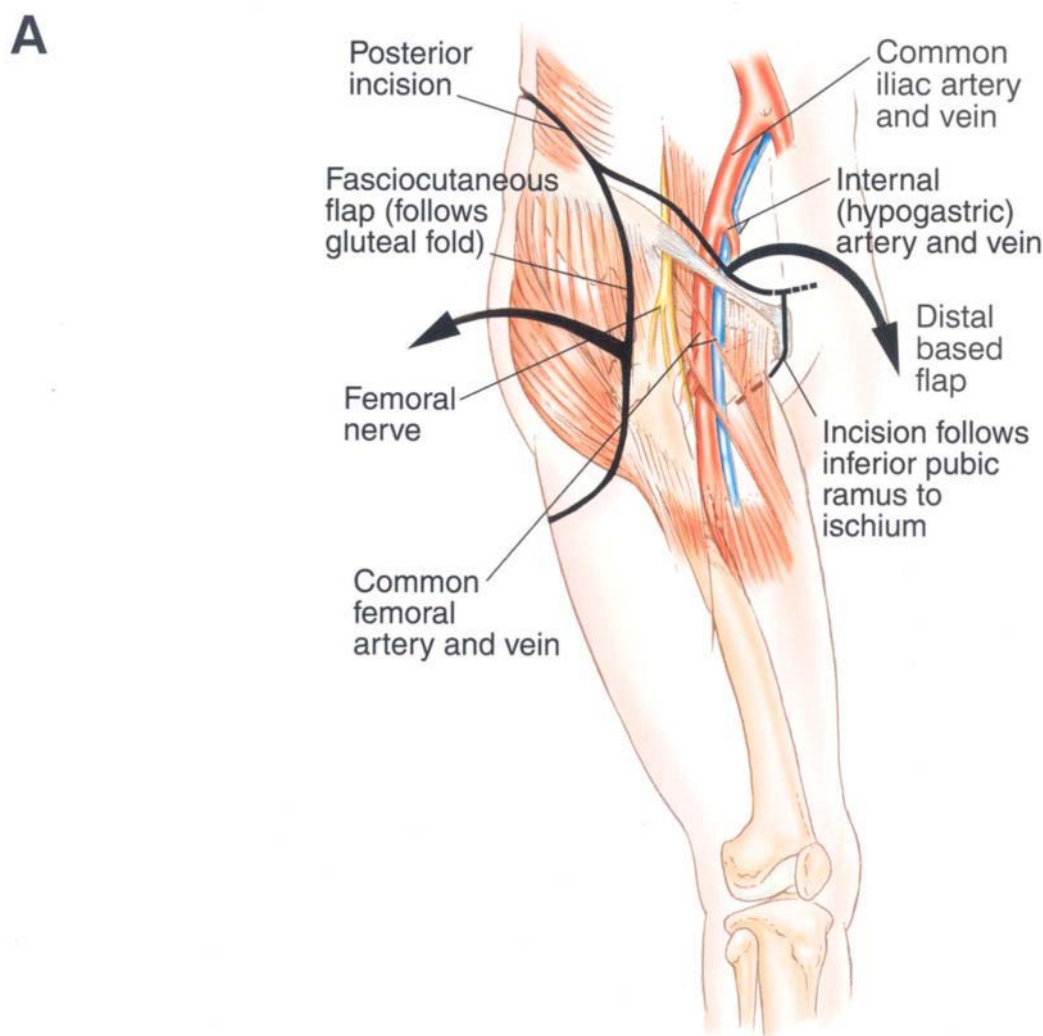
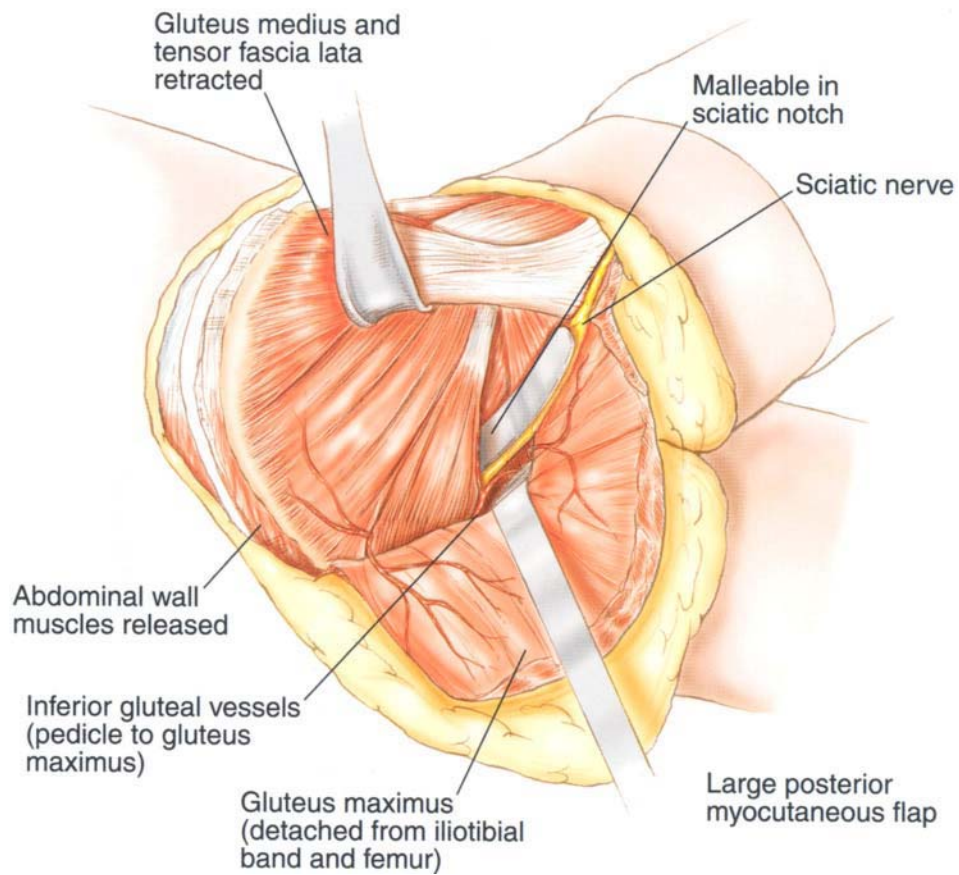
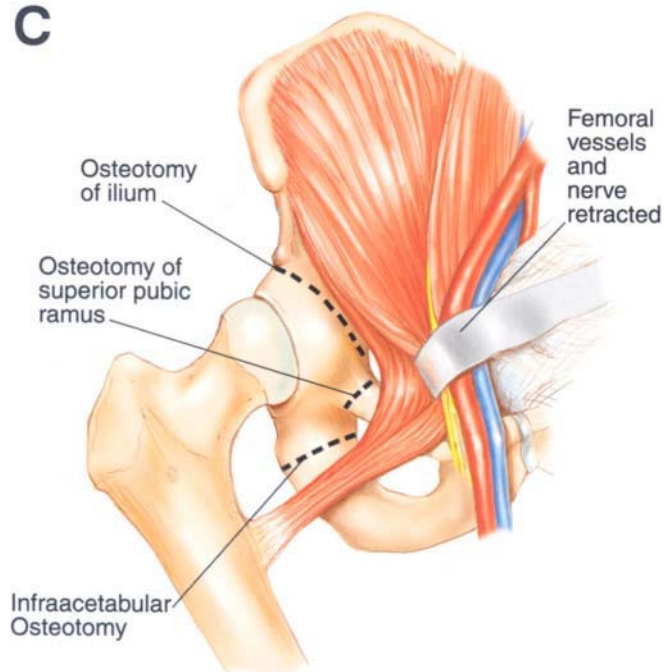


Figure 28.7 (see also following pages) **(A)** Surgical exposure. Utilitarian pelvic incision. The ilioinguinal incision permits exposure of the retroperitoneal space and mobilization of the iliac vessels, femoral nerve, and sciatic nerve. This permits exposure of the medial wall of the acetabulum as well as the ilium and the superior pubic ramus. **(B)** A large posterior fasciocutaneous flap based medially permits the release of the gluteus maximus. The gluteus maximus muscle is detached from the iliotibial band and the femur, and it is rotated posteriorly. This provides exposure of the ilium, sciatic notch, sciatic nerve, and hip joint. Through this posterior incision the proximal iliac osteotomy is performed, as well as ischial osteotomy. The periacetabular tumor is removed through this incision following the release of the sacrotuberous ligament. **(C)** Schematic diagram of the mobilization of the periacetabular structures and the three osteotomies which are necessary for a complete resection of the acetabulum. The superacetabular osteotomy is performed through the sciatic notch, the superior pubic ramus is transected at the level of the retracted femoral vessels, and the infra-acetabular osteotomy is performed above the level of the ischium. Once all three osteotomies are completed the acetabulum can be removed through the posterior incision by detaching the sacrospinous ligament. **(D)** Schematic of the "close-up" of the superior pubic ramus osteotomy. The femoral triangle and nerve are identified and retracted. The superior pubic ramus is identified and the pectineus muscle is transected. This permits exposure of the superior pubic ramus which is then protected by a Cobra retractor and is osteotomized with a high-speed drill. **(E)** (page 436) Schematic diagram of the infra-acetabular osteotomy. The osteotomy is performed through the posterior incision above the level of the origin of the biceps femoris. A Cobra retractor is inserted along the inferior border of the ischium and is placed into the obturator foramen in order to protect the adjacent soft tissues. Once these osteotomies are performed, the sacrospinous ligament can be palpated and released off of the spine. **(F)** (page 436) A notch is made in the supra-acetabular roof or remaining ilium for the saddle prosthesis to sit in. A high-speed burr is used. **(G)** (page 436) Schematic diagram of the saddle prosthesis reduced into the notch. The femoral stem is cemented into the femur. The size of the base element is chosen to make a tight fit on reduction. The greater trochanter is fixed with cables. The abductor and psoas muscle tension keeps the prosthesis reduced. **(H)** (page 436) Schematic diagram of the saddle prosthesis following a periacetabular resection (Type II) for a sarcoma and radical curettage for a large acetabular metastasis.

B



C



D

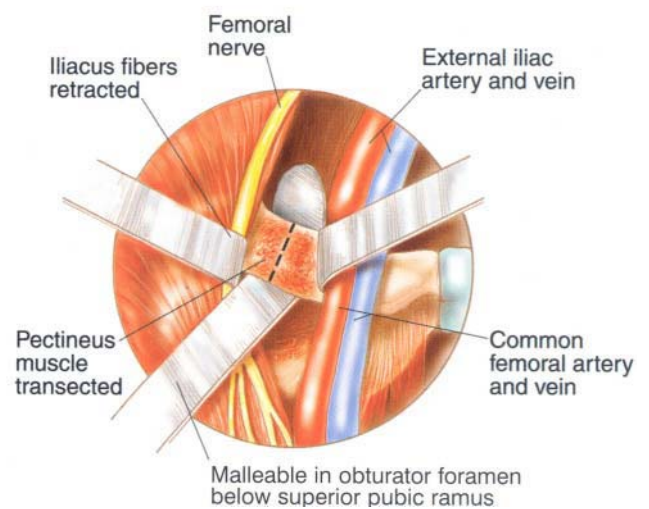


Figure 28.7 B-D

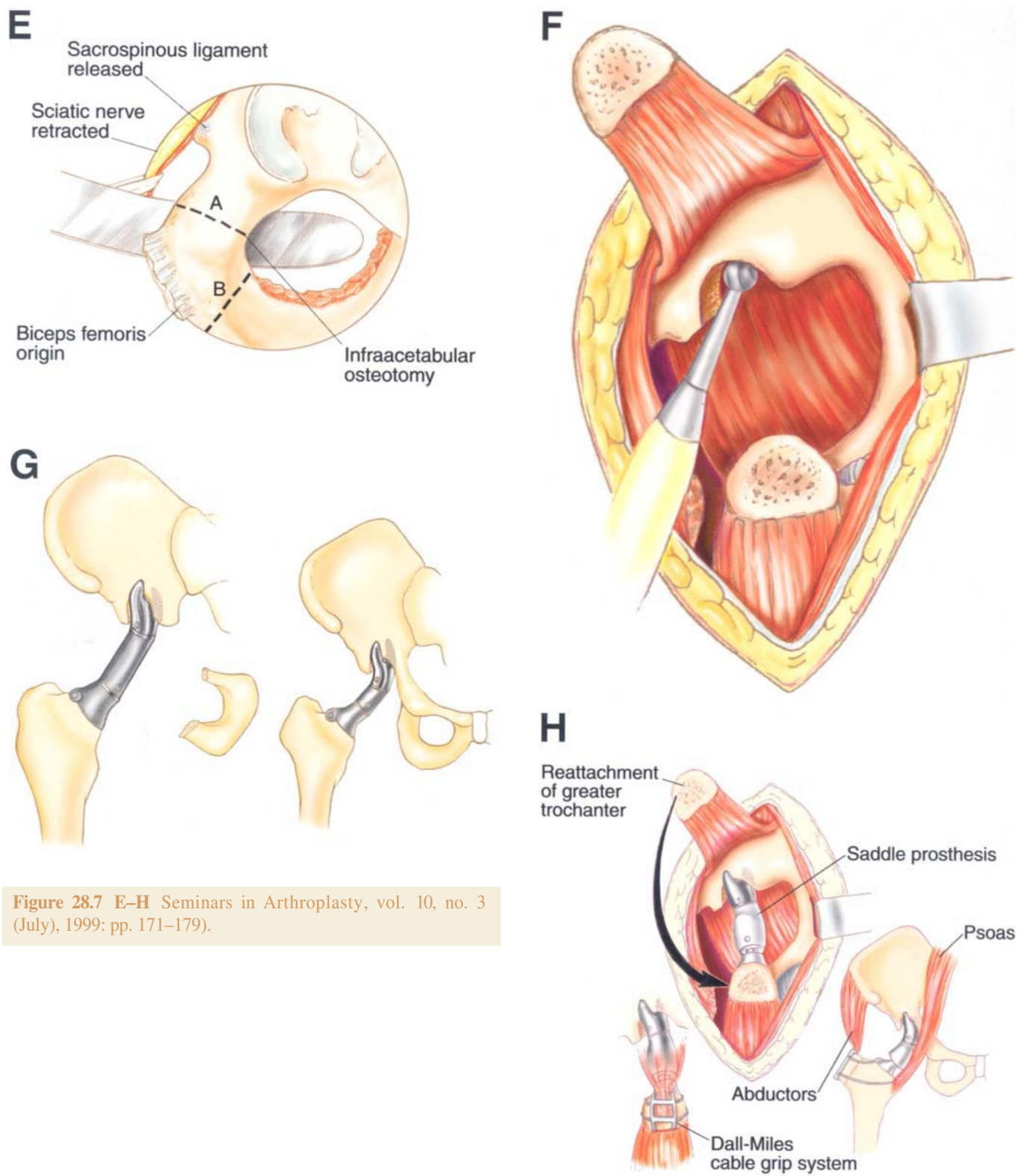


Figure 28.7 E–H Seminars in Arthroplasty, vol. 10, no. 3 (July), 1999: pp. 171–179).

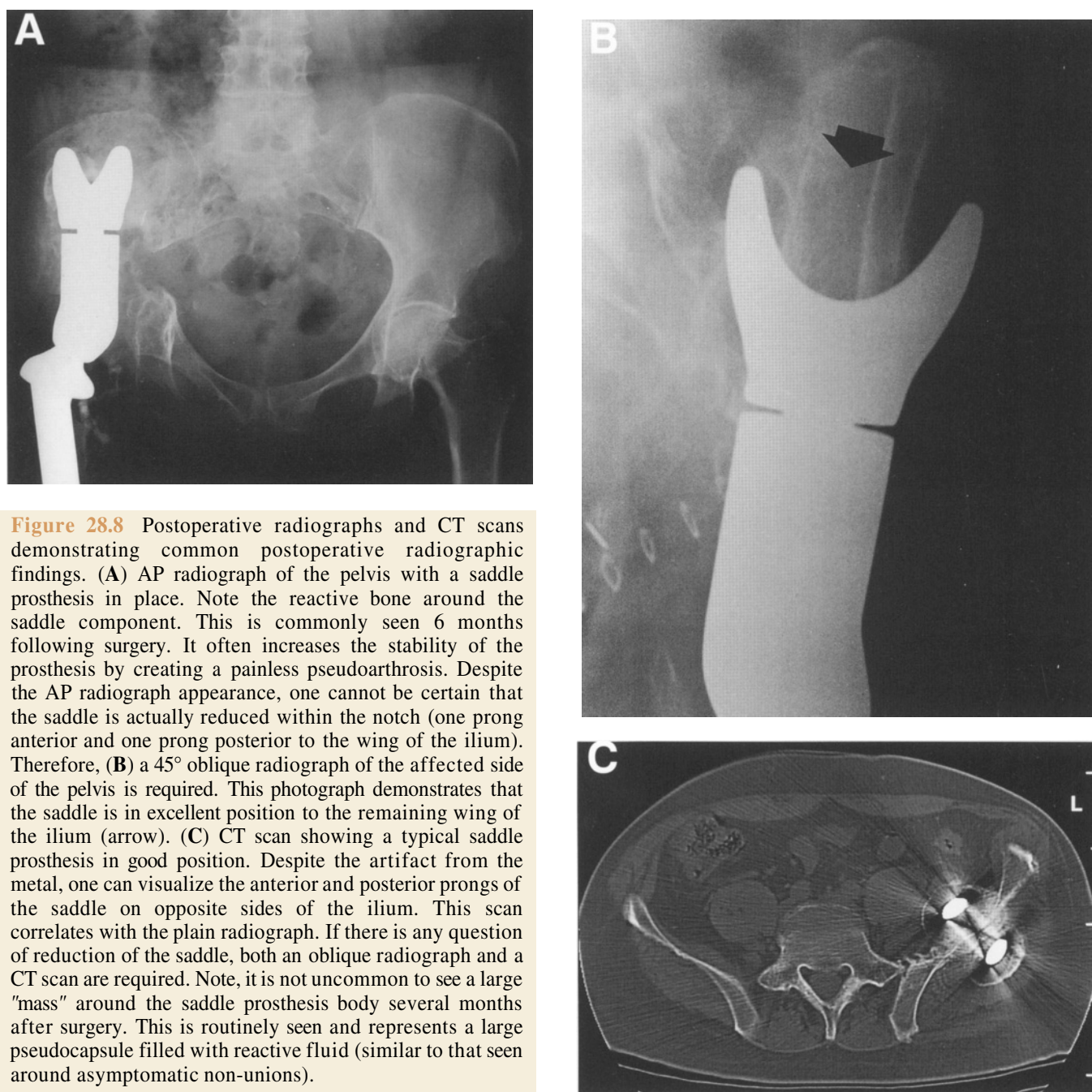


Figure 28.8 Postoperative radiographs and CT scans demonstrating common postoperative radiographic findings. (A) AP radiograph of the pelvis with a saddle prosthesis in place. Note the reactive bone around the saddle component. This is commonly seen 6 months following surgery. It often increases the stability of the prosthesis by creating a painless pseudoarthrosis. Despite the AP radiograph appearance, one cannot be certain that the saddle is actually reduced within the notch (one prong anterior and one prong posterior to the wing of the ilium). Therefore, (B) a 45° oblique radiograph of the affected side of the pelvis is required. This photograph demonstrates that the saddle is in excellent position to the remaining wing of the ilium (arrow). (C) CT scan showing a typical saddle prosthesis in good position. Despite the artifact from the metal, one can visualize the anterior and posterior prongs of the saddle on opposite sides of the ilium. This scan correlates with the plain radiograph. If there is any question of reduction of the saddle, both an oblique radiograph and a CT scan are required. Note, it is not uncommon to see a large "mass" around the saddle prosthesis body several months after surgery. This is routinely seen and represents a large pseudocapsule filled with reactive fluid (similar to that seen around asymptomatic non-unions).

reconstruction, and the overall condition of the patient.

Initially, patients who have undergone a periacetabular tumor resection and reconstruction are kept in bed with the operative extremity placed in balanced suspension. This provides more reliable elevation of the

extremity and minimizes mobility while the incision begins to heal. This is continued for 3–4 days or until the wound is checked and all of the drains removed. All wound drainage tubes are left in place until the drainage is less than 30–50 ml per 24 h period. Once the incision is healing, and the drains have been removed, the

patient is placed in a hip abduction orthosis with a pelvic band (if the hip abductors were reconstructed) and gait training is initiated.

Patients who have undergone a saddle prosthetic reconstruction begin ambulation with a walker or crutches, weight-bearing as tolerated. Although weight-bearing is progressed as tolerated, patients who have undergone a hip abductor repair are encouraged to protect the soft-tissue reconstruction (and remain in the

brace) for approximately 6 weeks. Initially, motion is encouraged within the limits of the brace (60 degrees of flexion, no extension, abduction, or adduction). Patients are encouraged to perform straight-leg raises and knee and ankle motion exercises. Once the brace is removed, range of motion is progressed and hip flexor and abductor strengthening is begun. Patients are instructed on "total hip precautions" and discouraged from flexing the hip greater than 90 degrees or crossing their legs.

Proximal and Total Femur Resection with Endoprosthetic Reconstruction

Jacob Bickels, Isaac Meller, Robert Henshaw and
Martin Malawer

OVERVIEW

Proximal and total femur resections are limb-sparing options for most primary bone sarcomas, metastatic lesions, and a variety of nononcologic indications of the proximal and midfemur that were traditionally treated with a major amputation. However, proximal and total femur resections are highly complex surgical procedures. Meticulous surgical technique and proper postoperative management are mandatory for local tumor control and acceptable functional outcome. This chapter emphasizes the indications for surgery, preoperative evaluation, and surgical concepts and technique.

INTRODUCTION

The proximal femur and midfemur are common sites for primary bone sarcomas; approximately 16% of Ewing's sarcomas,¹ 13% of chondrosarcomas,² and 10% of osteosarcomas³ develop at these locations. Metastatic tumors are the most common malignant lesions of the proximal femur, with carcinomas being the most frequent. The large majority of patients with metastatic lesions to the proximal femur respond well to radiation therapy. Of the 5–10% of these patients who require surgery, the most common reason is pathologic fracture, followed by tumor progression and intractable pain.

Patients who were candidates for extensive femoral resection because of malignant tumor were long considered a high-risk group for limb-sparing procedures because of the extent of bone and soft-tissue resection, as well as the use of adjuvant chemotherapy and radiation therapy. Hip disarticulation or hemipelvectomy was therefore the classic treatment for patients with large lesions of the proximal or midfemur. Both procedures were associated with a dismal functional and psychological outcome. Improved survival of patients with musculoskeletal malignancies, developments in bioengineering, and refinements in surgical technique have allowed the execution of limb-sparing surgeries in these extreme situations. As a result, proximal and total femur resection have become surgical options in the treatment of primary bone sarcomas and metastatic bone disease,^{4–7} as well as of a variety of nononcologic indications, including failure of internal fixation, severe acute fractures with poor bone quality, failed total hip, osteomyelitis, metabolic bone disease, and various congenital skeletal defects.^{8–10}

Methods of skeletal reconstruction include resection–arthrodesis,¹¹ massive osteoarticular allograft,¹² endoprosthetic reconstruction,^{13,14} and prosthetic–allograft composites.¹⁵ Osteoarticular allografts, which were popular in the 1970s and 1980s, attempt to restore the natural anatomy of a joint by matching the donor bone to the recipient's anatomy; however, over time they are associated with increased rates of infection, nonunion, instability, fracture, and subchondral collapse that lead to failure.^{16,17}

Custom-made prostheses were initially used for reconstruction. The early prostheses were manufactured on the basis of radiographic estimates of the intended surgical resection (Figure 29.1). The preoperative design and manufacturing process lasted 8–10 weeks. In the era before the use of neoadjuvant chemotherapy, this caused a significant delay in the timing of surgeries for bone sarcomas. A second drawback of custom-made prostheses is the difficulty in determining the actual length and width of the resected bone on the basis of

imaging modalities alone. Any deviation in the surgical plan, whether caused by underestimation of tumor extension or an error in the preoperative calculation, could jeopardize the planned reconstruction. Khong *et al.*¹⁸ reported a 13.1% incidence of oversized implants in 82 patients treated with 84 proximal femur resections.

Introduced in the mid-1980s, modular prostheses revolutionized endoprosthetic reconstruction.¹⁹ Components of these interchangeable systems include articulating segments, bodies, and stems in varying lengths and diameters. Design features include extensive porous coating on the extracortical portion of the prostheses for bone and soft-tissue fixation, as well as metallic loops to assist in muscle reattachment (Figure 29.2). The modular system enables the surgeon to measure the bone defect at the time of surgery and select the most appropriate components to use in reconstruction.¹⁹ Modular systems also provide an element of expandability that is invaluable for skeletally immature patients. Finally, standardization of the modular components permitted a significant reduction in manufacturing costs and allowed the implementation of quality-control techniques that could not be used for custom orders.

This chapter describes the surgical technique of proximal and total femur endoprosthetic reconstruction and emphasizes acetabular and joint capsule preservation, capsulorrhaphy around the prosthetic neck, and reconstruction of the abductor mechanism as means of restoring hip joint stability. Proximal and total femur resections are grouped together because the surgical technique around the proximal femur, which is the more complex aspect of the surgery, and concerns of joint stability, are similar.

PREOPERATIVE EVALUATION

Proximal femur resection is performed for metaphyseal–diaphyseal lesions that: (1) extend below the lesser trochanter, (2) cause extensive cortical destruction, and (3) spare at least 3 cm of distal femoral diaphysis (Figures 29.3–29.5). Total femur resection is performed for diaphyseal lesions that: (1) extend proximally to the lesser trochanter and distally to the distal diaphyseal–metaphyseal junction and (2) cause extensive bone destruction (Figures 29.6 and 29.7). Most metastatic lesions of the proximal femur can be treated with an intra-articular resection of the femoral head and neck and reconstruction with long-stem bipolar endoprosthesis. Resection is considered when: (1) the tumor is extremely large, (2) the tumor has progressed significantly in spite of radiation or chemotherapy, (3) a previous operative procedure has failed, and (4) the lesion is a solitary metastasis. Nononcologic indications for

proximal and total femur endoprosthetic reconstruction include failure of internal fixation, severe acute fractures with poor bone quality, failed total hip arthroplasty with segmental bone loss below the level of the lesser trochanter, chronic osteomyelitis, metabolic bone disease, and various congenital skeletal defects (Figures 29.8 and 29.9).

Proximal and total femur resections are major surgical procedures that necessitate a detailed preoperative evaluation. By means of physical examination and imaging studies the surgeon must determine: (1) the extent of bone resection and dimensions of the required prosthesis; (2) the extent of soft-tissue resection and reconstruction

possibilities; and (3) the proximity of the tumor to the femoral vessels, femoral nerve, and sciatic nerve. Most complications can be avoided by predicting them prior to surgery and modifying the surgical technique accordingly.

A full range of imaging studies is needed, including plain radiography, computed tomography (CT), and magnetic resonance imaging (MRI) of the whole femur and the hip and knee joints. CT and plain radiography are used to evaluate the extent and level of bone destruction, and MRI is used to evaluate the medullary and extraosseous components of the tumor. Three-phase bone scan is essential to determine the presence of metastatic bone disease.

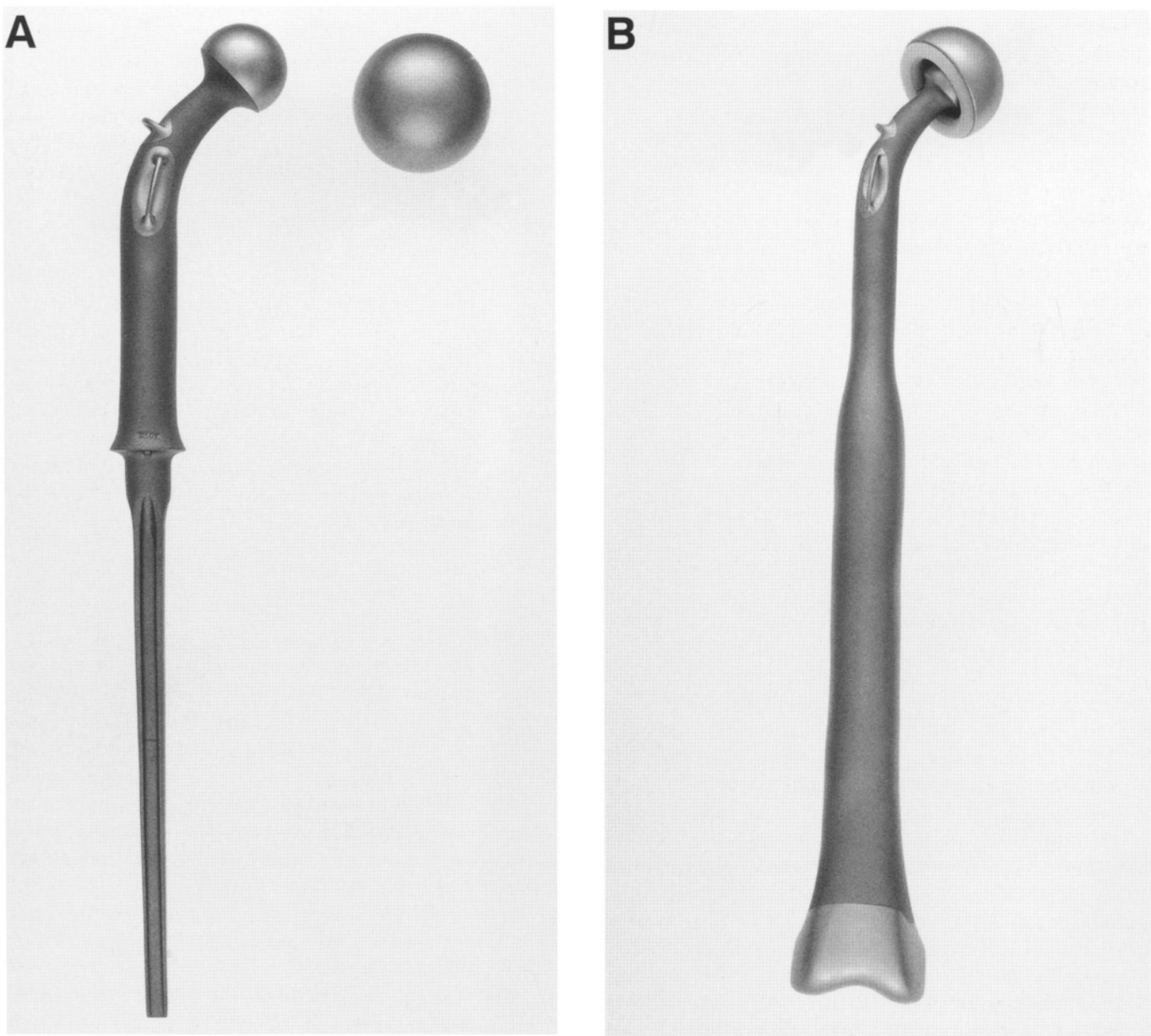


Figure 29.1 Custom-made prostheses. (A) Proximal femur, and (B) total femur (Howmedica, Rutherford, NJ).

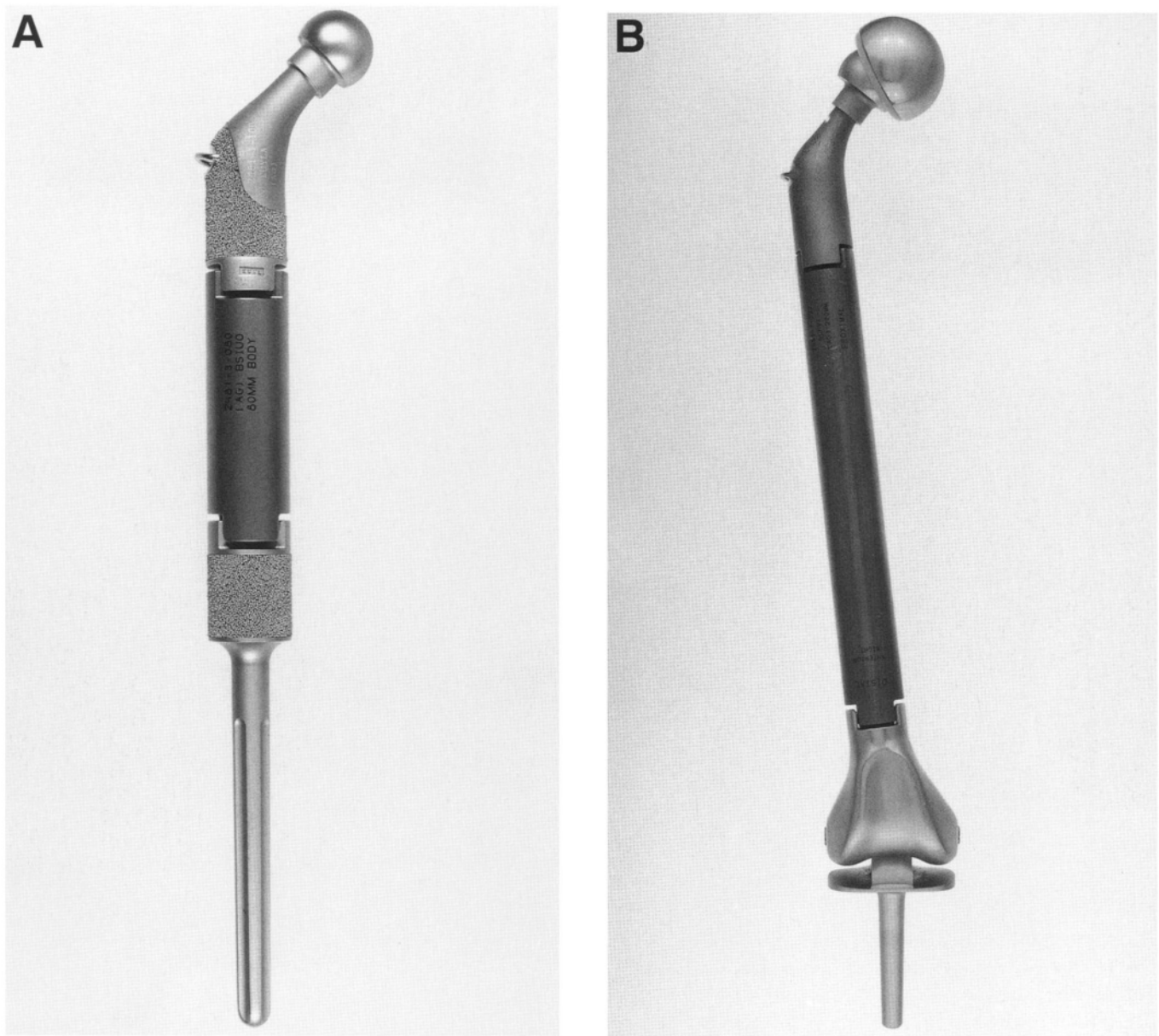


Figure 29.2 (see also following page) Modular prostheses. (A) Proximal femur, and (B) total femur (Howmedica, Rutherford, NJ). (C) Plain anteroposterior radiograph of the pelvis and lower extremities, showing a modular proximal femur prosthesis with a bipolar head in a 31-year-old patient with Ewing's sarcoma. The greater trochanter was spared and reconstructed with a cable grip system.

Angiography of the iliofemoral vessels is essential prior to resection of tumors of the proximal femur. Vascular displacement is common when tumors have a large, medial extraosseous component; the profundus femoral artery is particularly likely to be distorted or, less commonly, directly incorporated into the tumor mass. If the tumor has a large medial extraosseous component, and ligation of the profundus femoral artery is anticipated, a patent superficial femoral artery must be documented by angiography prior to surgery. Preoperative embolization may be useful in prepara-

tion for resection of metastatic vascular carcinomas if an intralesional procedure is anticipated. Metastatic hypernephroma is an extreme example of a vascular lesion that may bleed extensively and cause exsanguination upon the execution of an intralesional procedure without prior embolization.

In general, surgery for metastatic tumors to the proximal femur is practiced in the same manner as surgery for primary sarcomas of bone. The main differences are that metastatic lesions have a smaller extraosseous component than primary lesions, and the surrounding



Figure 29.2 C

muscles are usually invaded by the metastatic lesions (as opposed to the "pushing" border of bone sarcomas).²⁰ The intracapsular location of the femoral neck makes it biologically possible for tumors of the proximal femur to spread into the hip joint and adjacent synovium, hip capsule, and ligamentum teres. It also facilitates the possibility of extra-articular "skip" metastasis across the ligamentum teres into the acetabulum in the area of the fovea. Fortunately, intra-articular involvement is rare and usually occurs following a pathologic fracture. The capsule can therefore be preserved and an intra-articular resection of the femur performed in most cases. Fixed unipolar or bipolar heads are used because of the increased likelihood of hip dislocation following acetabular resurfacing.^{17,21} In the case of capsular or acetabular involvement, extra-articular resection of the hip joint is performed and a saddle prosthesis is used for reconstruction.²²

SURGICAL TECHNIQUE

Limb-sparing surgery that involves endoprosthetic reconstruction has three steps: tumor resection,



Figure 29.3 (above) Metastatic lesion of the proximal femur metaphysis that extends beyond the lesser trochanter; wide resection necessitates proximal femur resection.

endoprosthetic reconstruction, and soft-tissue reconstruction. The surgical technique of proximal femur resection with endoprosthetic reconstruction is described. The extra steps required for total femur resection are presented at the end of the appropriate sections.

Tumor Resection

Patient Positioning and Surgical Incision

The patient is placed in a lateral position on the operating room table to allow slight anterior and posterior rolling. A long posterolateral incision is made (Figure 29.10). This approach allows exposure of the proximal one-third of the femur, the retrogluteal area, and allows for identification of the superficial femoral



Figure 29.4 Osteosarcoma of the proximal femur. Following neoadjuvant chemotherapy the patient underwent proximal femur resection with endoprosthetic reconstruction.



Figure 29.5 Solitary lymphoma of the proximal femur. The patient underwent proximal femur resection with endoprosthetic reconstruction, followed by radiation therapy.

artery. An ilioinguinal extension to that incision is added if the tumor has an extensive, medial soft-tissue component along the proximal femur. This incision allows safe exposure of the femoral canal, femoral triangle, profundus femoral artery, and sartorial canal. *If total femur resection is performed*, the incision is brought distally to the anterolateral aspect of the patellar tendon and tibial tuberosity. If the tumor has a medial component along the distal femur, it is approached best through a medially curved incision (Figure 29.10, insert).

Gluteus Maximus and Medius Detachment

The iliotibial band is opened longitudinally to allow adequate anterior and posterior exposure and partial detachment of the femoral insertion of the gluteus maximus muscle. Posterior reflection of the gluteus maximus muscle allows ligation of the first perforating

artery, which is in intimate apposition with the gluteal tendon attachment. The gluteus maximus is then further retracted in a posterior direction, exposing the retrogluteal area, external rotators, sciatic nerve, abductors, and posterior capsule (Figure 29.11). The sciatic nerve lies directly posterior to the external rotators. In general, as primary bone sarcomas expand, the external rotators are pushed outward and act as a protective barrier to the sciatic nerve. In these patients the sciatic nerve is therefore often not in its usual anatomic location. To prevent nerve damage it must be identified early, isolated, and mobilized posteriorly. The abductors are identified with their anterior and posterior intervals. If there is no tumor involvement, the greater trochanter is osteotomized; otherwise the abductors are transected through their tendinous attachments and retracted, exposing the hip joint and acetabulum (Figure 29.11, insert).



Figure 29.6 Large Ewing's sarcoma of the entire femoral diaphysis, presenting with a pathologic fracture. Following neoadjuvant chemotherapy the patient underwent total femur resection with endoprosthetic reconstruction.

Vastus Lateralis Reflection

The vastus lateralis is reflected distally from its origin, and the posterior perforating vessels are ligated (**Figure 29.12**). The vastus lateralis has to be preserved because of its future role in soft-tissue coverage of the prosthesis; it will be advanced proximally and sutured to the abductors (see section on Soft-tissue Reconstruction). Care is taken not to ligate its main pedicle, which crosses anteriorly and obliquely along the rectus femoris fascia.

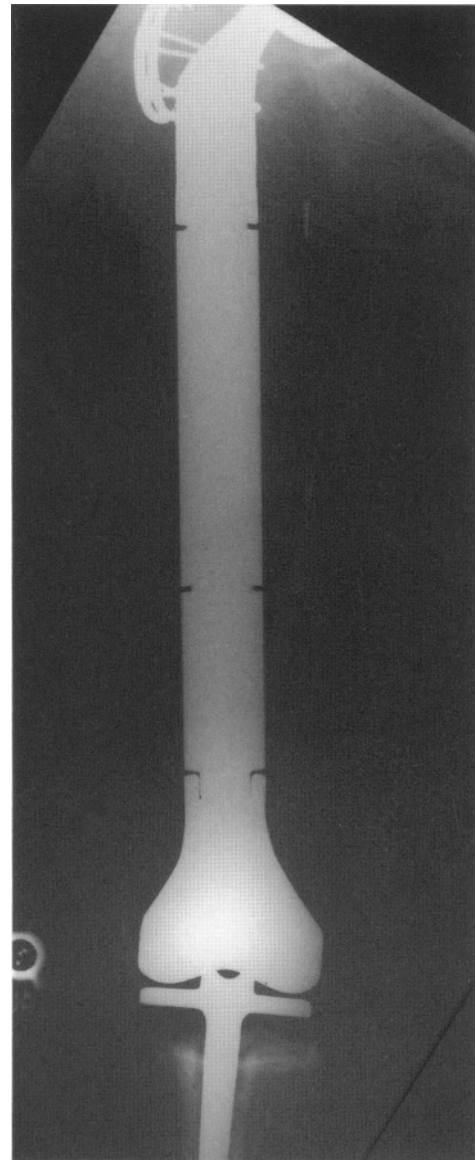


Figure 29.7 Postoperative radiograph showing the final total femur prosthetic reconstruction of the patient shown in **Figure 29.6**.

Although the major neurovascular bundle is usually not involved by metastatic lesions of the proximal femur, it is often displaced by large medial extraosseous extension of primary bone sarcomas. In that case the neurovascular bundle must be identified and mobilized. The lateral interval of the sartorius muscle is opened, exposing a portion of the iliacus muscle as it passes over the superior pubic ramus. The femoral nerve is identified below the fascia (**Figure 29.12**). The superficial and profundus femoral artery and vein are identified in the sartorial canal and retracted. The profundus artery and vein may be ligated just distal to their takeoff from the common femoral vessel.

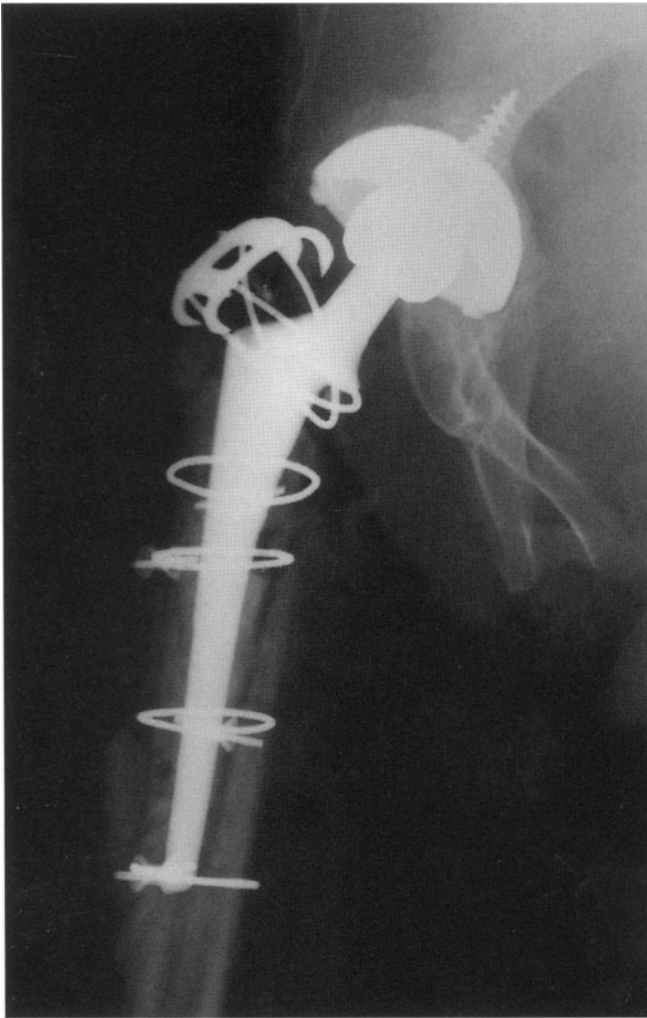


Figure 29.8 Plain radiograph of infected total hip arthroplasty. A proximal femur resection was performed, and the bone defect was reconstructed with a temporary spacer, composed of proximal femur prosthesis wrapped with cement and antibiotics. Following a prolonged course of intravenous antibiotics the spacer was replaced by a fixed cemented proximal femur prosthesis.

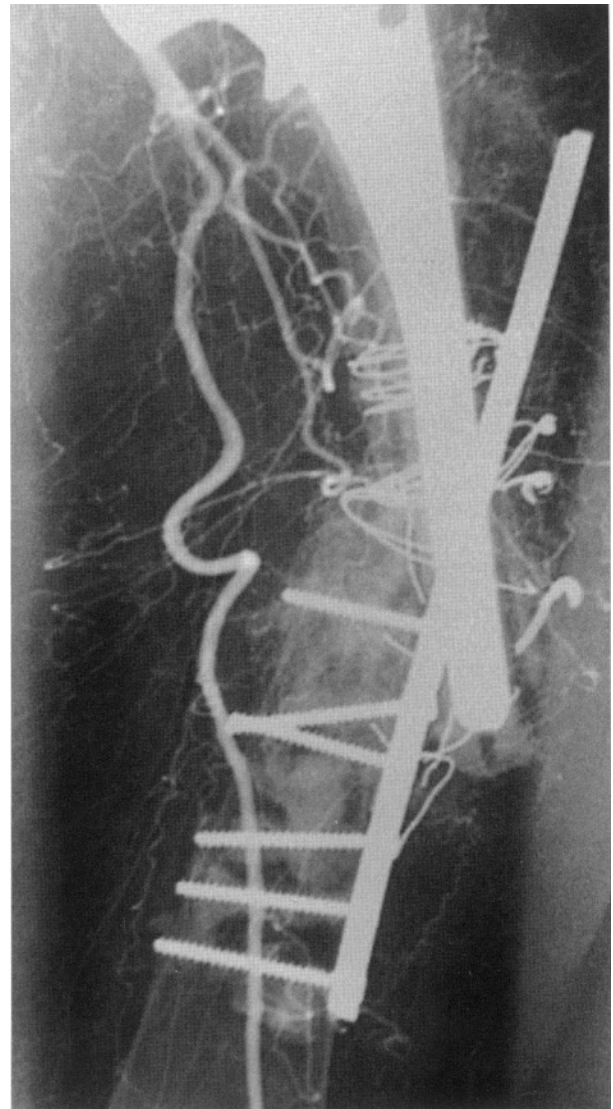


Figure 29.9 Extensive periprosthetic failure of internal fixation with a significant deformity and major functional deficit. Total femur resection and reconstruction with a modular prosthesis were performed.

Detachment of Posterior Hip Musculature and Capsule

The retrogluteal area has been previously exposed. The rotator muscles are now detached en-bloc 1 cm from their insertion on the proximal femur. The hip joint capsule has a major role in securing and stabilizing the head of the prosthesis within the acetabulum and, if not invaded by tumor, it should remain intact and be left as a separate plane. The capsule is opened longitudinally along its anterolateral aspect and detached circumferentially from the femoral neck (Figure 29.13). *If total femur resection is performed*, through an anterolateral arthrotomy, the cruciate ligaments,

collateral ligaments, and menisci, as well as capsular and muscular attachments to the distal femur, are resected (Figure 29.14). The popliteal vessels, tibial nerve, and peroneal nerve are identified and mobilized prior to arthrotomy of the knee joint. The total femur is resected en-bloc with the vastus intermedius muscle; the vastus lateralis, rectus femoris, patella, and patellar tendon are preserved. Marcove *et al.*⁷ reported a series of patients who underwent total femur resection. To preserve the extensor mechanism, they maintained the patellar tendon and split the patella in a coronal fashion so that the inner half remained with the surgical specimen and the outer half

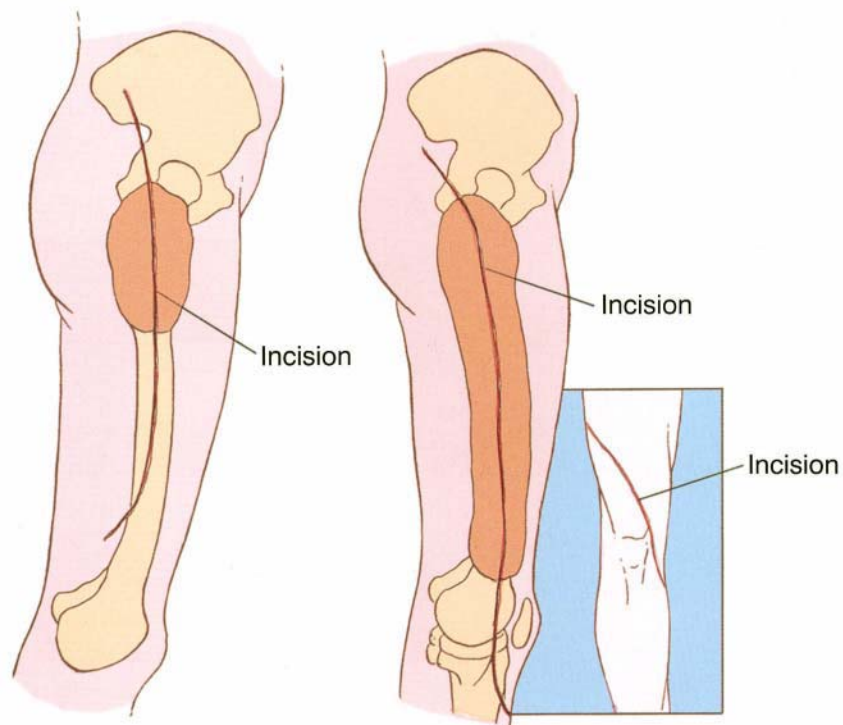


Figure 29.10 A posterolateral incision is routinely used for proximal femur resections. If a total femur resection is performed, the incision is extended to the anterolateral aspect of the patellar tendon. If there is a medial component of the tumor in the distal femur, the incision is curved to the medial aspect of the distal femur and knee joint. (Clin Orthop 2000 Jun (375):218–230)

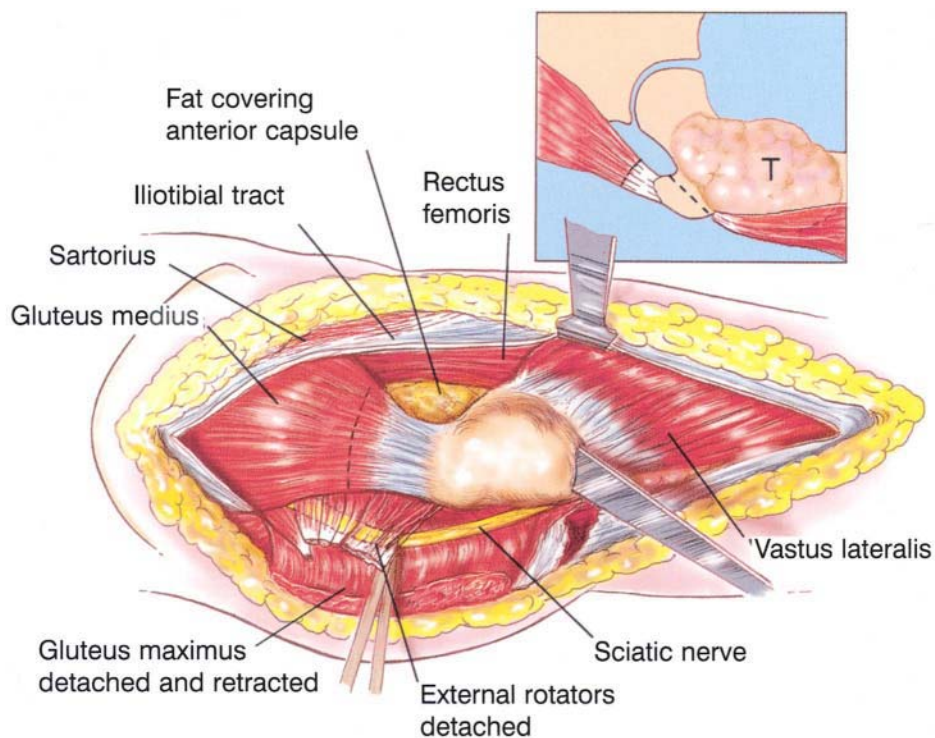


Figure 29.11 Detachment of posterior reflection of the gluteus maximus muscle. Identification of the sciatic nerve and detachment of abductor musculature. (Clin Orthop 2000 Jun (375):218–230)

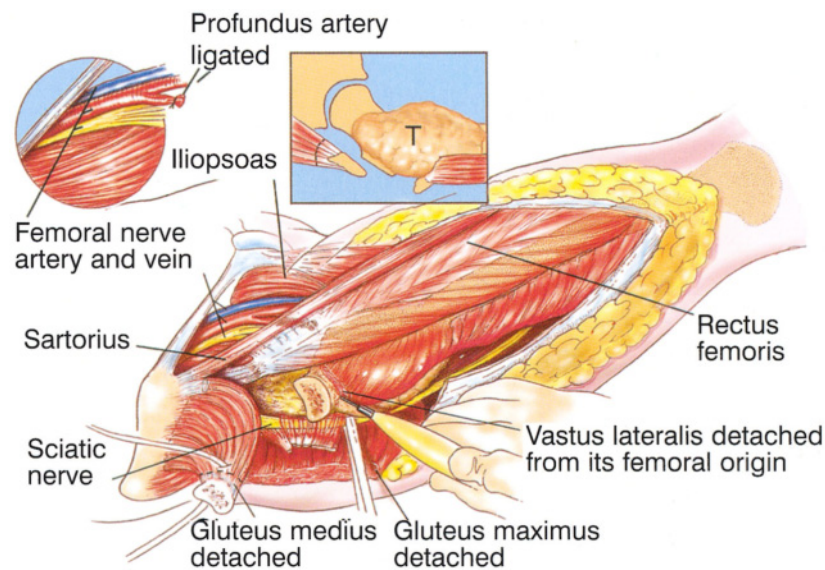


Figure 29.12 Reflection of the vastus lateralis muscle. Exploration and mobilization of the neurovascular bundle, if necessary.

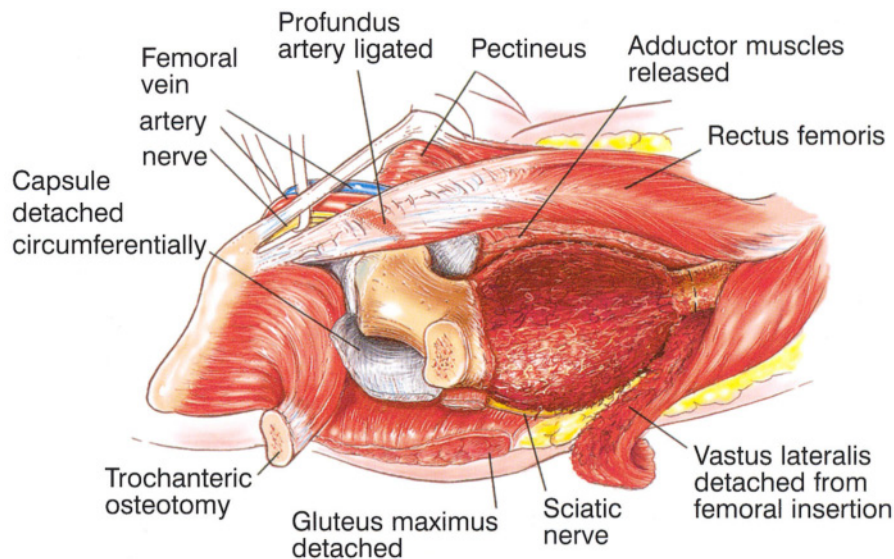


Figure 29.13 Detachment of the posterior hip musculature and capsule. (Clin Orthop 2000 Jun (375):218–230)

remained in continuity with the retained extensor mechanism. Malignant tumors of the distal femur rarely penetrate the vastus intermedius muscle or patellar surface; therefore the patella can be preserved in the large majority of the cases.

Dislocation of the Femur

The femur is dislocated anterolaterally. Care is taken not to fracture the femoral neck, especially if a primary bone sarcoma is being resected. The acetabulum is inspected for evidence of joint involvement.

Distal Femur Osteotomy

Femoral osteotomy is performed at the appropriate location, as determined by the preoperative imaging studies. In general, 3–4 cm beyond the farthest point is appropriate for primary sarcomas and 1–2 cm for metastatic carcinomas. An oscillating saw is used for the osteotomy and a malleable retractor is placed medially to the femoral shaft to prevent inadvertent injury to the soft tissues. The cut should be at a right angle to the shaft (Figure 29.15). It is important not to distract the extremity following removal of the proximal femur, in

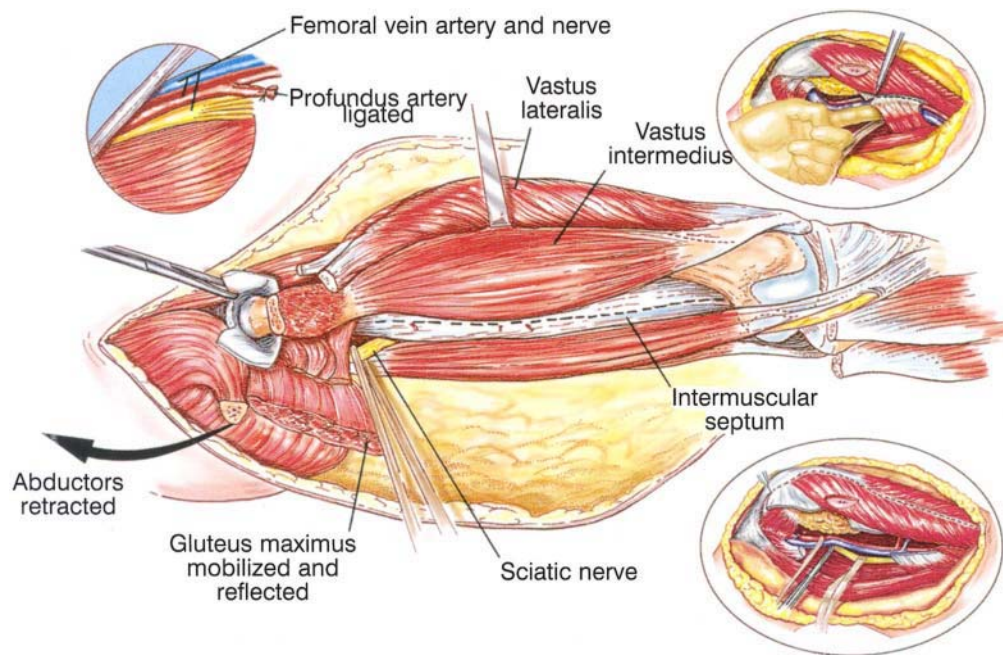


Figure 29.14 As in distal femur resection, the popliteal vessels, tibial nerve, and peroneal nerve are identified and mobilized prior to arthrotomy of the knee joint.

order to avoid placing tension on the sciatic nerve and femoral vessels. *If total femur resection is performed*, a tibial osteotomy is performed in the same manner as a standard knee joint arthroplasty. Approximately 1 cm of bone is removed; the cut is perpendicular to the long axis of the tibia. The insertion of the biceps femoris muscle is retained. It may be divided during resection and subsequently sutured.

Release of Medial Structures

Following femoral osteotomy or disconnection of the entire femur after tibial osteotomy, the femur is retracted laterally. The remaining medial structures are now clearly visible; these consist of the psoas and adductor muscles, which should be identified at this point or before the femur is osteotomized. They are serially dissected, clamped with Kelly clamps, and tagged with Dacron tapes. Care is taken to dissect the profundus femoral artery. If oncologically indicated, and only after patency of the superficial femoral artery was documented, the profundus femoral artery may be ligated.

Endoprosthetic Reconstruction

Following resection of the proximal femur, the length of the femur, the size of the femoral head, and the

diameter of the distal medullary canal are measured. A trial femoral head prosthesis is utilized to test the suction fit. The proximal end of the remaining femur should be kept well padded to avoid injuring the superficial femoral artery. Prior to reaming the femoral canal a frozen section from the canal is evaluated for evidence of residual tumor.

Reaming the Intramedullary Canal

The largest possible stem diameter should be chosen. A 1-mm cement mantle is required around the stem. The intramedullary canal is therefore reamed 2 mm larger than the chosen stem diameter (Figure 29.16).

Trial Articulation

Three parts must be assembled to articulate the proximal femoral component and match the length of the resected specimen: neck, body, and head (Figure 29.17). Total femur prostheses are mated to the tibial component via a rotating hinge mechanism (Figure 29.18). Following trial positioning of the prosthesis, the pulses are palpated distally; if diminished, a shorter prosthesis is required. The joint capsule is pulled over the femoral head component, and the range of motion of the hip joint is tested. The prosthesis should be stable in flexion, adduction, and internal rotation.

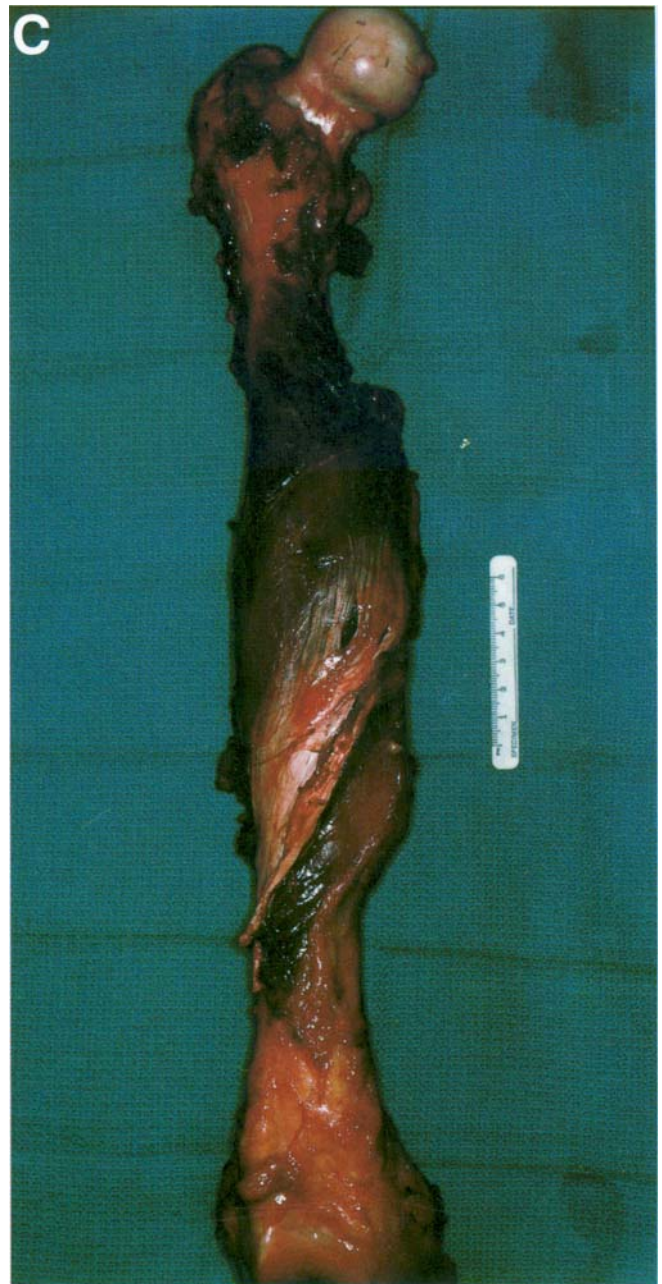
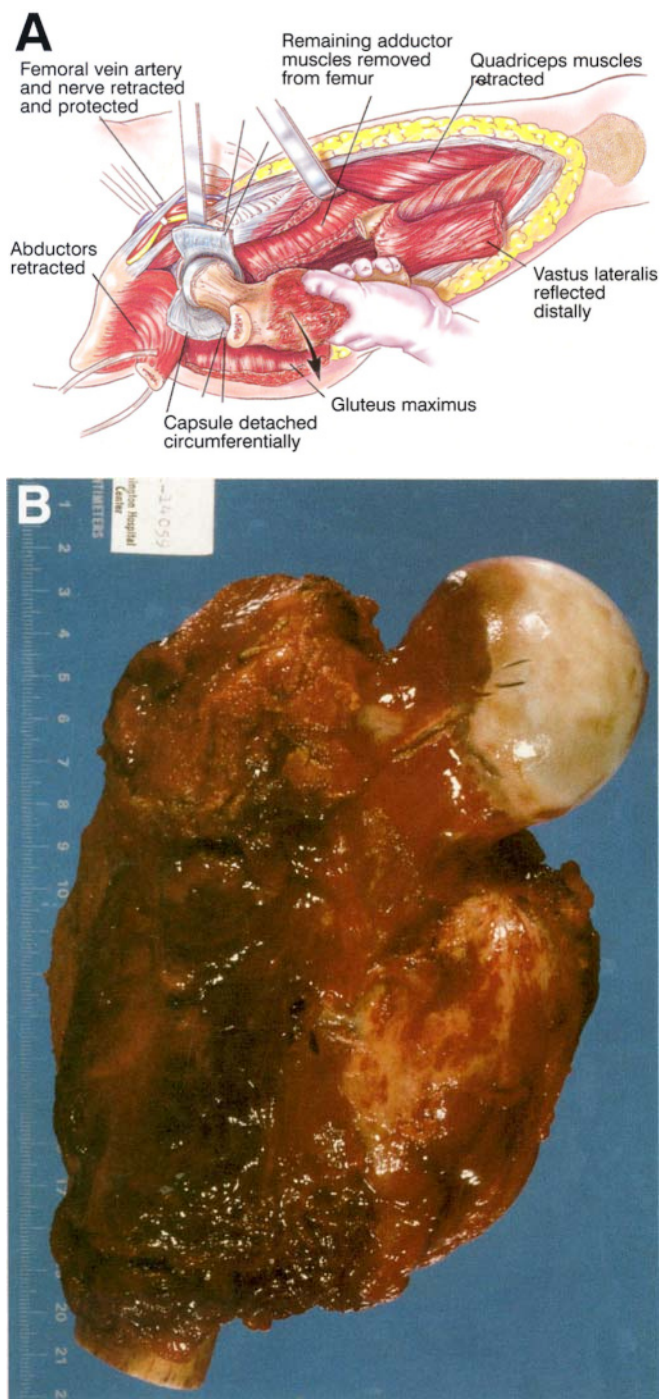


Figure 29.15 (A) Femur osteotomy; surgical specimens: (B) proximal femur, and (C) total femur.

Prosthetic Assembly and Implantation

The modular prosthesis is assembled and cemented into the medullary canal. The orientation of the prosthesis is critical. With the linea aspera as the only remaining anatomic guideline the prosthesis is placed with the femoral neck anteverted about 5–10° with

respect to an imaginary perpendicular line from the prosthesis and a line drawn from the linea aspera through the body of the prosthesis (Figure 29.19). Leg length is evaluated and the neurovascular bundle is assessed again for excessive tension. Patellar resurfacing is not routinely performed in patients who undergo total femur resection because its contribution to the

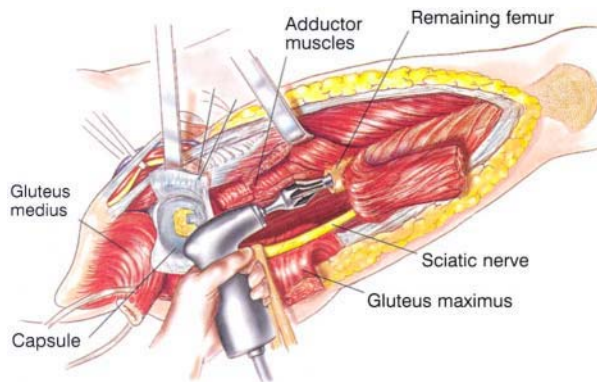


Figure 29.16 Reaming of the intramedullary canal.

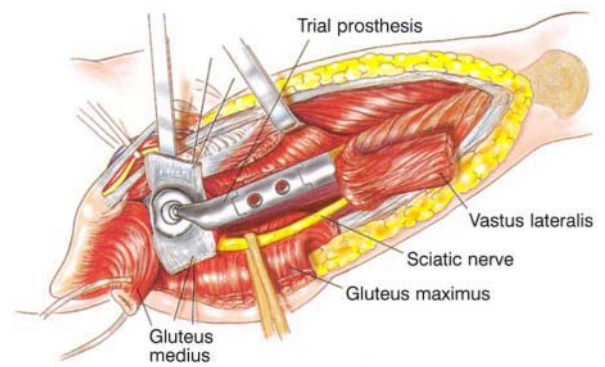


Figure 29.17 Trial articulation. Leg length must be evaluated and neurovascular bundle assessed for excessive tension.

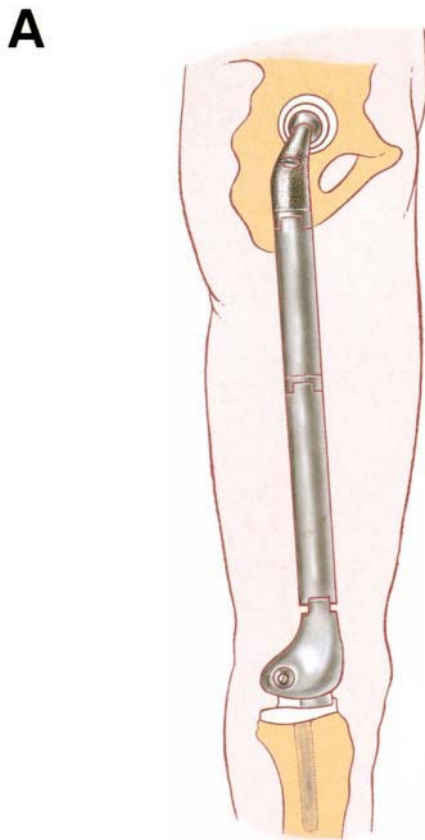
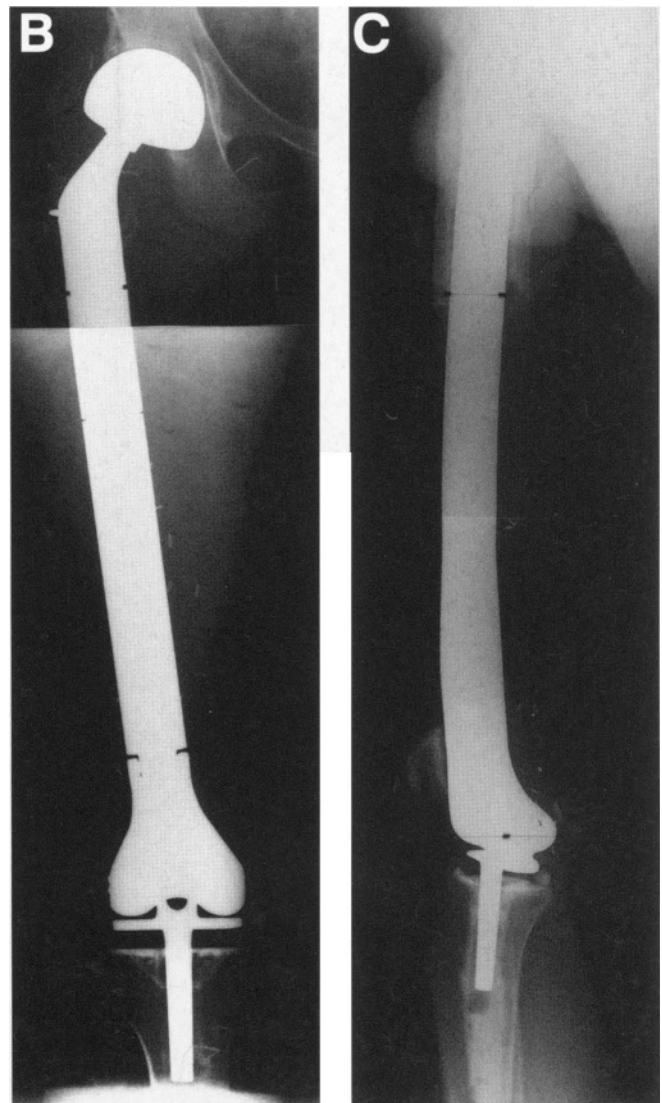


Figure 29.18 (A) Schematic of a total femur prosthesis. This is mated to the tibial component via a rotating hinge mechanism. Plain radiographs, (B) anteroposterior and (C) lateral views, of total femur prosthesis with a rotating hinge knee mechanism (Howmedica, Rutherford, NJ).



functional outcome is questionable,^{23,24} and because most patients with primary sarcoma of bone are young and have minimal degenerative changes in the patellofemoral joint.

Cementation

A third-generation cementing technique, which involves pulsatile lavage, use of intramedullary cement restrictor, reduction of the cement by centrifugation, use of a cement gun, pressurization of the cement, and enhancement of the prosthesis–cement interface by precoating the proximal portion of the femoral or tibial stem with bone cement, is employed.²⁵ While the bone cement hardens, the surgeons continuously verify the correct positioning of the prosthesis.

Soft-tissue Reconstruction and Extracortical Bone Fixation

Special attention is given to re-establish hip and knee joint stability and provide adequate muscle coverage of the prosthesis. This allows good function and prevents contamination and deep periprosthetic infection, should there be a superficial wound infection or dehiscence.

Reconstruction of the Hip Capsule

Once the prosthesis is cemented into place, the remaining hip capsule is sutured with a 3-mm Dacron tape (Deknatel, Falls River, MA) around the neck of the prosthesis. This forms a noose around the neck of the prosthesis and provides immediate stability (Figures 29.19B insert, 29.20 and 29.21). Dacron is a nonabsorbable synthetic polyester (polyethylene terephthalate) that allows approximation of the cut ends of the joint capsule under significant tension, and provides the initial mechanical support which is required for scarring of the capsule. When the capsule is adequately closed, the surgeon cannot dislocate the prosthesis. The capsule is reinforced by rotating the external rotator muscles proximally and suturing them to the repaired capsule. The remaining psoas muscle is rotated anteriorly to close and reinforce the capsular repair.

Extracortical Bone and Soft-tissue Fixation

The extracortical component of the prosthesis can be utilized for additional bone and soft-tissue fixation in the form of a noose around the prosthesis. Bone struts are circumferentially held with Dacron tapes to the prosthesis–host bone interface (Figure 29.22). Theoretically, this will prevent debris from entering the

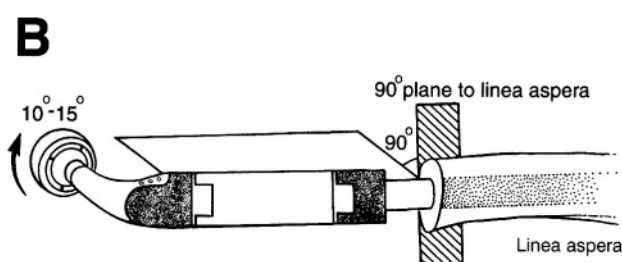


Figure 29.19 (A) Assembly of the definitive modular prosthesis. It should match the length of the resected specimen. Note the bipolar head and the rotating hinge knee mechanism. (B) The prosthesis is positioned in 5–10° of anteversion with the linea aspera being the only remaining anatomic guideline for proximal femur endoprosthetic replacements and the tibial tuberosity for total femur endoprosthetic replacements.

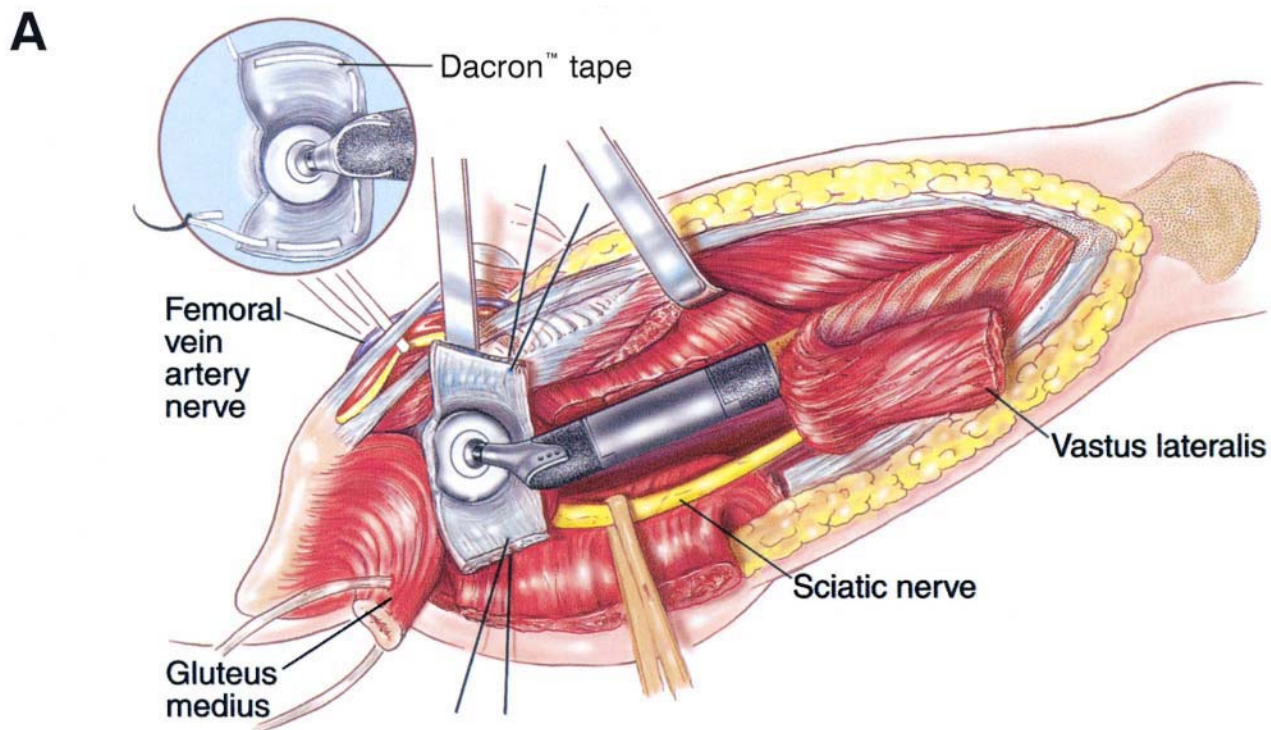


Figure 29.20 (A) The remaining capsule is brought over the head and neck of the prosthesis. This is reinforced by circumferential Dacron tape. (B) Operative photograph showing Dacron capsular reconstruction (arrow) prior to complete closure of capsule. (C) Completion of Dacron capsular repair. Note the head and neck of the prosthesis are completely closed by this reconstruction (arrows). The prosthesis should not be dislocatable at this stage. (Clin Orthop 2000 Jun (375):218–230)

bone–cement interface and reduce the possibility of aseptic prosthetic loosening (Figure 29.23).^{26,27}

Reconstruction of the Abductor Mechanism

If the greater trochanter was resected en-bloc with the surgical specimen, the remaining abductors may be brought down to the proximal aspect of the prosthesis and attached to a metal loop with a Dacron tape (Figure

29.22). If a fragment of the greater trochanter remains, it can be fixed to the prosthesis with a cable grip system (Figure 29.24). The vastus lateralis is rotated proximally to overlie the abductor muscle fixation. The remaining muscles are sutured to the vastus lateralis anteriorly and the hamstrings posteriorly. The hip and knee are tested for stability, the degree of which should guide the postoperative management. If total femur resection is performed and a soft-tissue defect exists around the knee

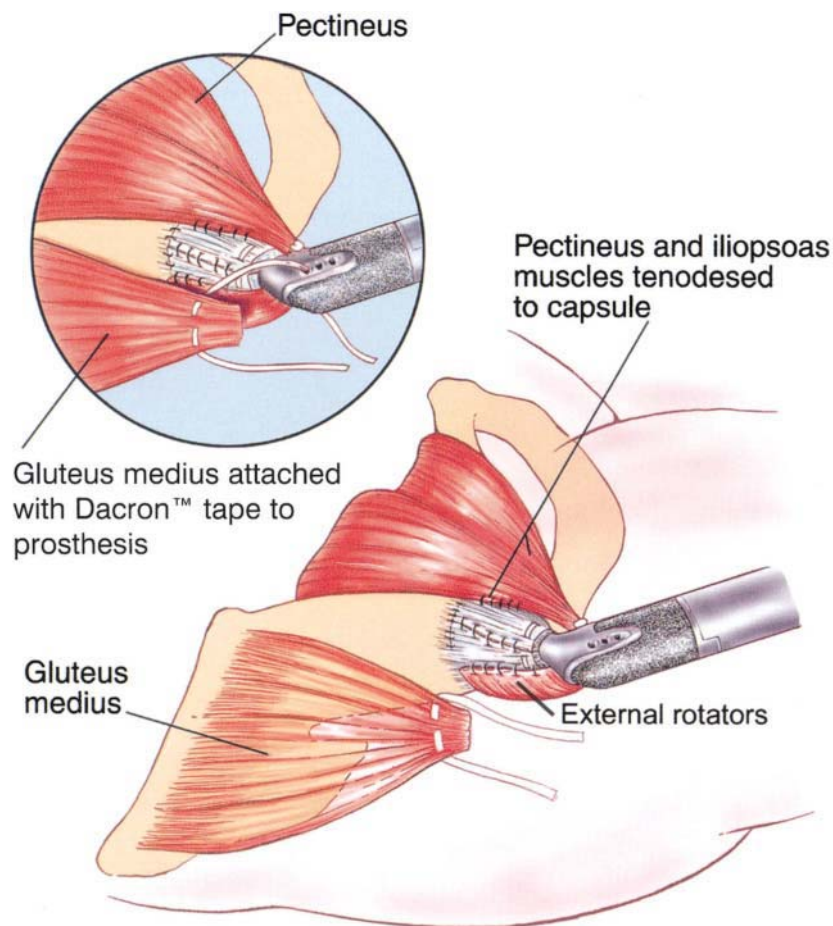


Figure 29.21 The capsule is tightly sutured with a 3-mm Dacron tape. When the capsule is adequately closed, the surgeon cannot dislocate the prosthesis. The capsule is then reinforced by tenodesing the pectineus and psoas muscles to the anterior capsule and the external rotators to the posterior capsule. The abductors are then advanced to the prosthesis with Dacron tape and tenodesed to the vastus lateralis muscle.

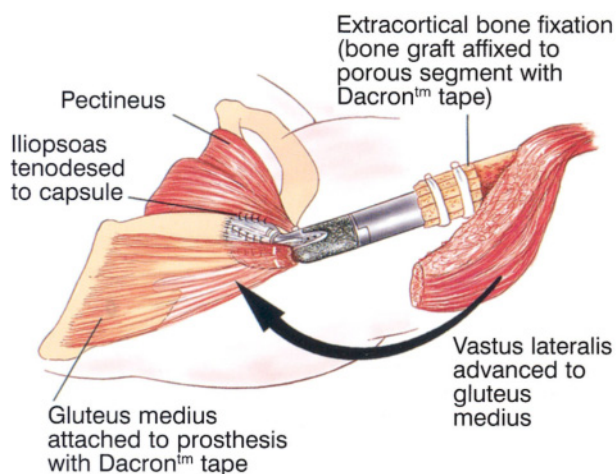


Figure 29.22 Extracortical bone fixation. Bone struts are circumferentially held over with Dacron tapes over the prosthesis–host bone interface.

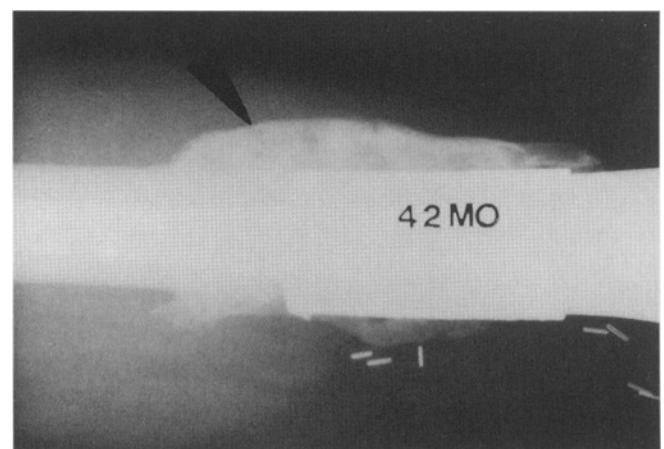


Figure 29.23 Thick rim of bone bridges the prosthesis–host bone interface (arrow); 42 months following proximal femur endoprosthetic reconstruction and extracortical bone fixation.

joint, an interposition gastrocnemius flap can be performed.²⁸

Wound Closure

The wound is closed over a 28-gauge chest tube that is attached to a continuous suction and superficial Jackson–Pratt drains (Figure 29.25). The pulse is checked following wound closure and prior to removing the patient from the table. The patient is then placed in balanced suspension and the hip is elevated and abducted in 20°.

Postoperative Management

1. To prevent postoperative edema and prosthetic dislocation the extremity is kept elevated and abducted in balanced suspension for at least 5 days. When swelling around the hip and thigh is resolved, an abduction brace is customized for the patient.
2. Continuous suction is required for 3–5 days after surgery to prevent fluid collection. Perioperative intravenous antibiotics are administered until the drainage tubes are removed.
3. Isometric exercises are started on the day after surgery.
4. Postoperative mobilization with an abduction brace and partial weight-bearing are required for about 3–4 weeks, depending on the extent of the soft-tissue resection and satisfactory soft-tissue reconstruction. Active hip abduction is required before the brace is removed and full weight-bearing allowed.

DISCUSSION

Preservation of the acetabulum and hip joint capsule and capsulorrhaphy over the prosthetic head are major factors in stabilization and prevention of dislocation. Stability is also enhanced by attaching of the abductors and psoas muscle to the prosthesis. There is a greater tendency for hip dislocation after massive proximal femur resection than after total hip arthroplasty, in which the abductor mechanism is preserved.^{29,30} It is therefore important that these muscles be preserved following resection. Muscle group tenodesis provides a balanced tension from the lateral and medial aspects of the femur, reinforces stability, and allows range of motion.²² A final factor in stabilization is the formation of scar tissue that bridges the joint capsule and adjacent musculature. In early series, in which capsular preservation was not emphasized, joint stability was based on muscle reconstruction and scar formation. Patients were placed in a long-leg brace with a pelvic band or skeletal traction from 6 weeks to 5 months.^{4,7}

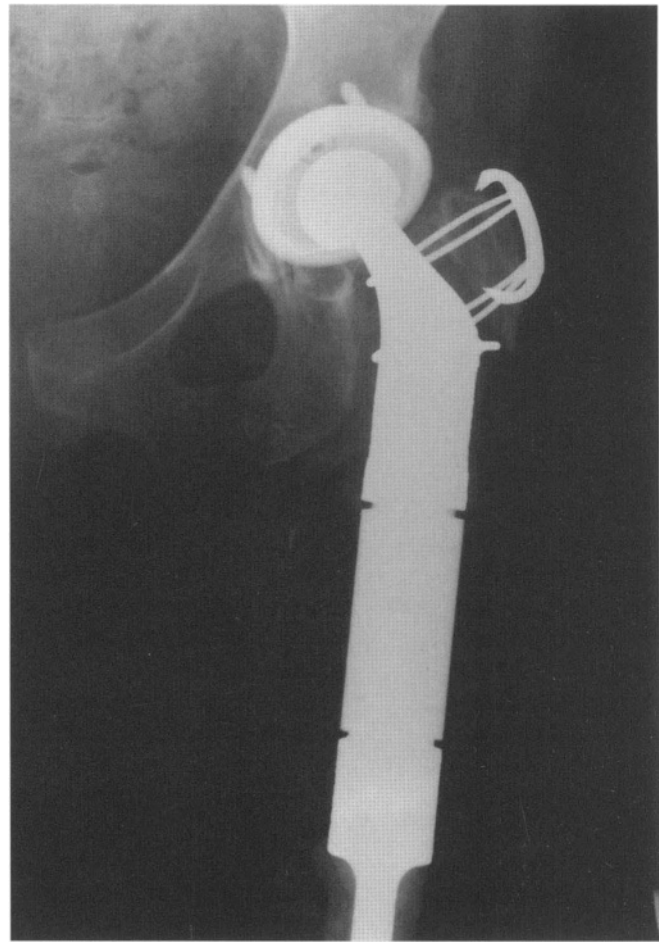


Figure 29.24 A proximal femur endoprosthetic reconstruction in a 35-year-old patient, performed as a two-stage salvage procedure for infected total hip arthroplasty. The greater trochanter and acetabular component were spared, and reconstruction of the abductor mechanism was performed with a cable grip system.

Dislocation is the most frequent complication following proximal and total femur resection, ranging from 11% to 14%.^{17,21,31,32} Malkani *et al.*¹⁰ reported a series of 50 proximal femur endoprosthetic reconstructions performed in 49 patients for nononcologic indications. Dislocations were the most common complication; they occurred in 11 patients (22%), four of whom required revision surgery. This dislocation rate is exceedingly high, considering that proximal femur resections for nononcologic indications require minimal soft-tissue resection. It is therefore easier to achieve adequate soft-tissue coverage and prosthetic stability than following those resections which are performed for malignant

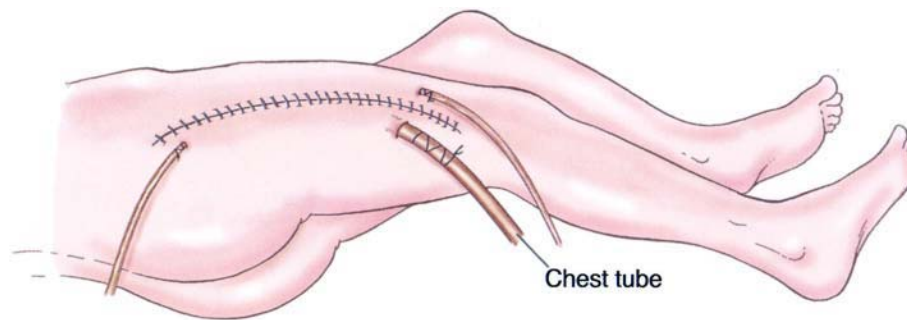


Figure 29.25 Surgical wound is closed over a deep-seated chest tube and superficial Jackson–Pratt drains.

tumors. Kabukcuoglu *et al.*³² reported 54 patients who underwent proximal femur resection with endoprosthetic reconstruction. In that series an attempt was made to preserve the joint capsule, but the acetabulum was resurfaced and no attempt was made to repair the hip abductors to the prosthesis; instead, they were sutured to the fascia lata.³² They reported six dislocations (11%), two of which necessitated surgical revision.³² Bickels *et al.* reported a series of 64 patients who underwent proximal or total femur endoprosthetic reconstruction with emphasis on the three elements of re-creating joint stability: preservation of the acetabulum, preservation of joint capsule and capsulorrhaphy, and, finally, reconstruction of the abductor mechanism to the neck of the prosthesis.³³ Only one patient in that series (1.6%) had a dislocation.

There have been few reports on the longevity of proximal femur replacement prosthesis. Dobbs *et al.*³⁴ reported 81 patients who underwent proximal femur resection and reconstruction with custom-made prostheses. Event-free survival rates were 73% and 63% at 5 and 10 years, respectively. Unwin *et al.*³⁵ reported a series of 263 patients who underwent proximal femur resection with endoprosthetic reconstruction. They reported a 93.8% probability that patients would not experience aseptic loosening during the 10 years following surgery. This rate compares favorably with the 67.4% and 58% survival rates of distal femur and proximal tibia endoprosthetic reconstruction, respectively.³³ The favorable outcome of proximal femur replacements was also noted by Horowitz *et al.*,¹³ who hypothesized a positive correlation between prosthetic survival and the availability of soft tissue for coverage. Aseptic loosening of proximal femur prostheses was

found to be highest when the percentage of the removed bone was low; there were no incidents of aseptic loosening following resection of more than 60% of the bone length.³⁵ The main factor underlying this phenomenon may be the extent of cement interdigitation, which is related to the amount of cancellous bone and the shape of the medullary canal. For short proximal femoral replacements much of the stem is within the reamed canal, where the amount of cancellous bone is minimal and cement interdigitation is poor. In long proximal femur replacements, on the other hand, a significant part of the stem is located within the flared canal and the metaphysis, where the amount of cancellous bone is sufficient to achieve adequate cement penetration.³⁵ The use of extracortical bone fixation over the prosthesis–host bone interface has a role in prevention of aseptic loosening and is practiced by the authors in all endoprosthetic reconstructions.

SUMMARY

Proximal and total femur resections with endoprosthetic reconstruction are complex surgical procedures that usually are executed in orthopedic oncology referral centers. Preoperative evaluation and planning, meticulous surgical technique, and adequate postoperative management are essential. Preservation of the acetabulum and joint capsule, Dacron tape capsulorrhaphy, and reconstruction of the abductor mechanism are major determinants of joint stability. Because of their safety and good functional outcome, such resections can also be used for a large variety of nononcologic indications, especially for major revision surgeries and persistent infections.

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Distal Femoral Resection with Endoprosthetic Reconstruction

Martin Malawer

OVERVIEW

The distal femur (Figure 30.1) is the most common site of osteosarcoma. Patients with osteosarcoma of the distal femur have traditionally been treated with a high above-knee amputation or hip disarticulation. Today, with earlier diagnosis and induction chemotherapy, approximately 95% of osteosarcomas can be resected with tumor-free margins. Careful preoperative evaluation and strict adherence to established criteria for resection of bone cancers are required to minimize the risk of local recurrences. Prosthetic reconstruction of the distal femur is an option that must be considered in all these patients. Use of the modular segmental replacement system (MRS) can provide limb salvage in many patients. The functional results are excellent, and patient satisfaction is high. The prosthesis has an excellent long-term survival rate, is reliable, and presents minimal problems of breakage or dysfunction.

This chapter describes in detail the preoperative staging, use of imaging studies, and the surgical technique of popliteal exploration, femoral resection, and prosthetic and soft-tissue reconstruction.

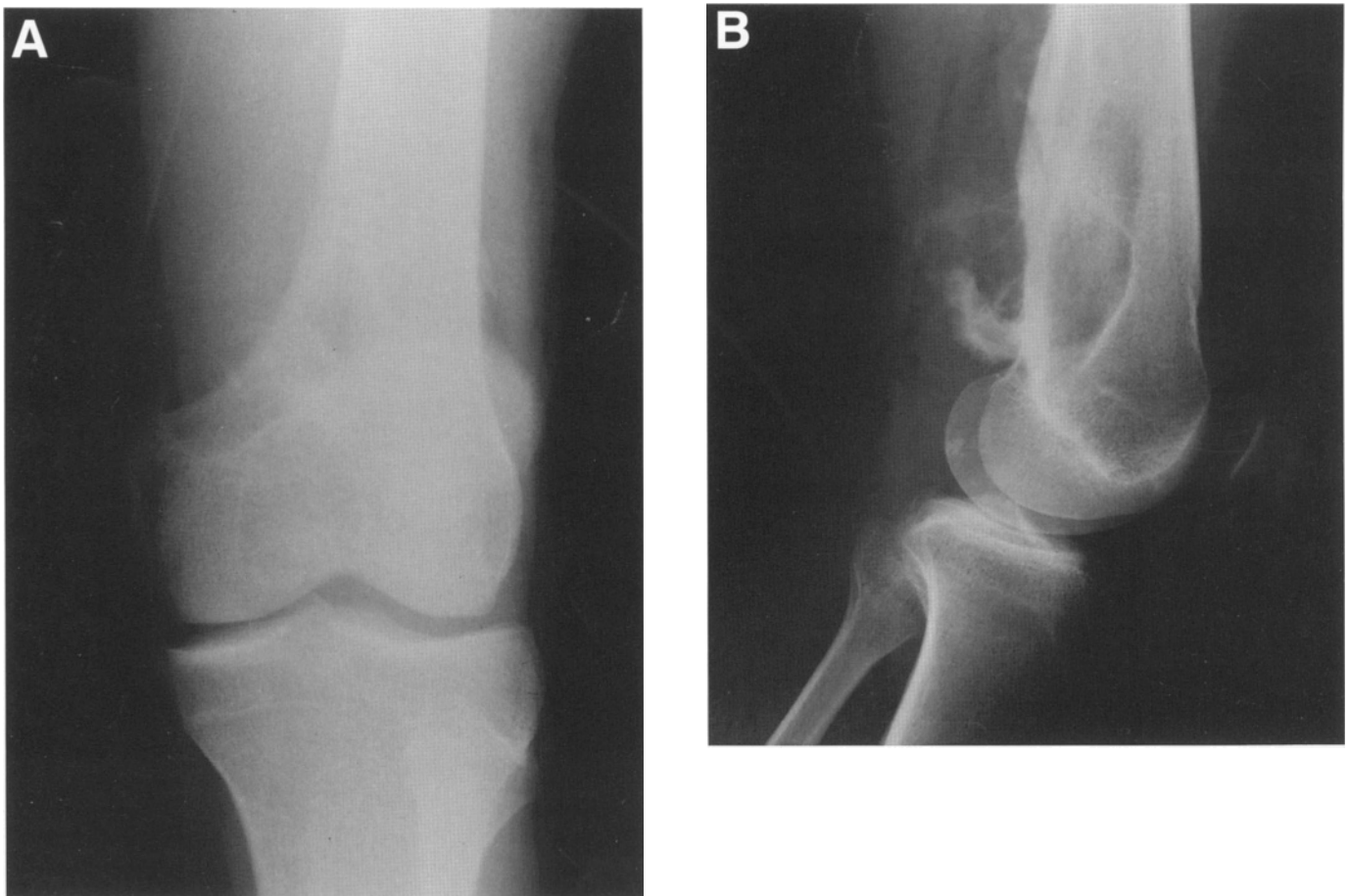


Figure 30.1 Plain radiograph showing a large osteolytic osteosarcoma arising from the posterior medial aspect of the distal femur. The distal femur is the most common location for osteosarcomas. A purely osteolytic lesion represents approximately 25% of all osteosarcomas. Most radiographic studies underestimate the extent of these lesions. (A) Anterior–posterior view of distal femur; (B) lateral view showing a large posterior component.

INTRODUCTION

Many recent studies have demonstrated a low risk of local recurrence (<5%) following limb-sparing surgery of osteosarcomas.^{1–5} The continuous disease-free survival rates in patients who have undergone resection are the same as or better than those of patients undergoing amputation; presumably because of the use of appropriate selection criteria. Eckardt *et al.*⁶ reported their experience at the University of California at Los Angeles with Stage IIB osteosarcoma for the period 1972–84. Seventy-eight of 116 patients (67%) were treated by a limb-sparing procedure and the local recurrence rate was 8%.⁶ Simon *et al.*⁷ compared results of limb-sparing procedures with those of amputation in 277 patients with osteosarcoma of the distal femur and found no difference between the two groups in the rate

of metastasis or local recurrence.⁷ Malawer *et al.*⁸ reported a 6% local recurrence rate following limb-sparing resections.

Because of the encouraging results reported in these and other studies, limb-sparing surgery is now considered the preferred treatment for carefully selected patients with osteosarcomas and other high-grade sarcomas involving the distal femur. Amputations are reserved principally for patients whose primary tumor is unresectable. The most common factors necessitating an amputation are significant contamination of the tumor site resulting from a poor biopsy, fracture, or extensive neurovascular involvement.⁸ The size and extent of the tumor are important only to the degree that they affect these three factors and influence the amount of soft tissue required to be resected, and thus the functional outcome. Even tumors with large

extraosseous components can be resected, in conjunction with most of the musculature of the distal thigh. If there is insignificant quadriceps remaining to power a prosthesis, hamstrings transfers can be performed or a primary arthrodesis performed. Muscle power is not necessary, because the "knee" will not bend.

The success of limb-sparing surgery has been dramatically improved by the use of induction (preoperative) chemotherapy. Today, most multidrug regimens are effective in "killing" the tumor, shrinking its size, and improving the surgical margins obtainable. The median tumor necrosis with these multidrug regimens is 90–95%.

UNIQUE ANATOMIC CONSIDERATIONS

The specific anatomic sites to be evaluated by the preoperative staging studies and their implication on resection technique are as follows:

Knee Joint

The knee joint is rarely directly involved by sarcoma. The main mechanisms of knee joint contamination are inappropriate biopsy, extension of tumor along the intra-articular cruciate ligaments, and pathologic fracture. Occasionally the tumor may cross the knee joint extra-articularly by following the capsular mechanism to the proximal tibial side. The knee joint can reliably be evaluated by computed tomography (CT) and magnetic resonance imaging (MRI). If the physical examination reveals any evidence of effusion, the knee joint should be aspirated and histologic samples obtained. A hemarthrosis usually indicates tumor involvement of the synovium. This is a rare event, but not an indication for amputation.

Popliteal Space

The popliteal space contains the popliteal artery and vein and the sciatic nerve. The popliteal vessels enter the popliteal space from the medial aspect through the adductor hiatus as the vessels exit the sartorial canal. The popliteal vessels are evaluated by CT with contrast, MRI, and plain angiography (Figure 30.2). It is rare to have direct vessel involvement by tumor. The vessels may be displaced as the tumor increases in size posteriorly, but usually there is a normal border or margin of popliteal fat. Exploration of the popliteal space is the first step in determining the feasibility of a limb-sparing procedure. The popliteal vessels are dissected out and the geniculate vessels are ligated. If the vessels are free of tumor, resection can usually be performed safely. A frozen section of the popliteal fat or adventitia of the popliteal vessels should be obtained intraoperatively. If

there is obvious vascular involvement the vessels can be replaced by vascular graft. The popliteal vein is usually not repaired since it rarely stays patent following surgery.

Sartorial Canal

The sartorial canal occupies the space between the vastus medialis, sartorius, and adductor magnus muscles in which the superficial femoral artery passes through the medial aspect of the thigh (adductor hiatus) and then enters the popliteal space. In patients whose tumors are greater than 13 cm in length, the sartorial canal is often displaced. The vessels within the canal are usually protected by the deep fascia of the vastus medialis and a tough fascia surrounding the vessels. This fascial border is rarely penetrated by tumor. Biopsies of the distal femur should avoid the sartorial canal, as well as the popliteal space and knee joint.

Anterior and Posterior Cruciate Ligaments

The cruciate ligaments are occasionally involved by direct tumor extension from the distal femur. This occurs through the bone-tendinous junction of the intercondylar notch of the distal femur. There is no cartilage in this area to act as a barrier for tumor growth. MRI is occasionally helpful in determining cruciate ligament involvement. Tumor nodules of the anterior and posterior cruciates occasionally can present with a hemarthrosis. The most common finding at the time of resection is tumor nodule involvement of the cruciates. This does not rule out a limb-sparing procedure. The cruciate ligaments as they attach to the proximal tibial plateau can be resected en-bloc with the proximal tibial cut. This is a safe procedure that avoids the need for a true extra-articular resection.

Preoperative staging studies focus on these four anatomic structures in order to allow the surgical team to determine the type of surgery, placement of the incision, the need for intra- or extra-articular resection, and biopsy technique and site.

PREOPERATIVE EVALUATION AND STAGING STUDIES (Figure 30.2)

Staging studies should be performed before biopsy if the plain radiographs suggest a malignant tumor.⁹ Preoperative studies allow the surgeon to conceptualize the local anatomy and appreciate the volume of tissue to be resected en-bloc, and the extent of surgical reconstruction that will be needed. The biopsy site can subsequently be planned according to the anticipated surgical approach.

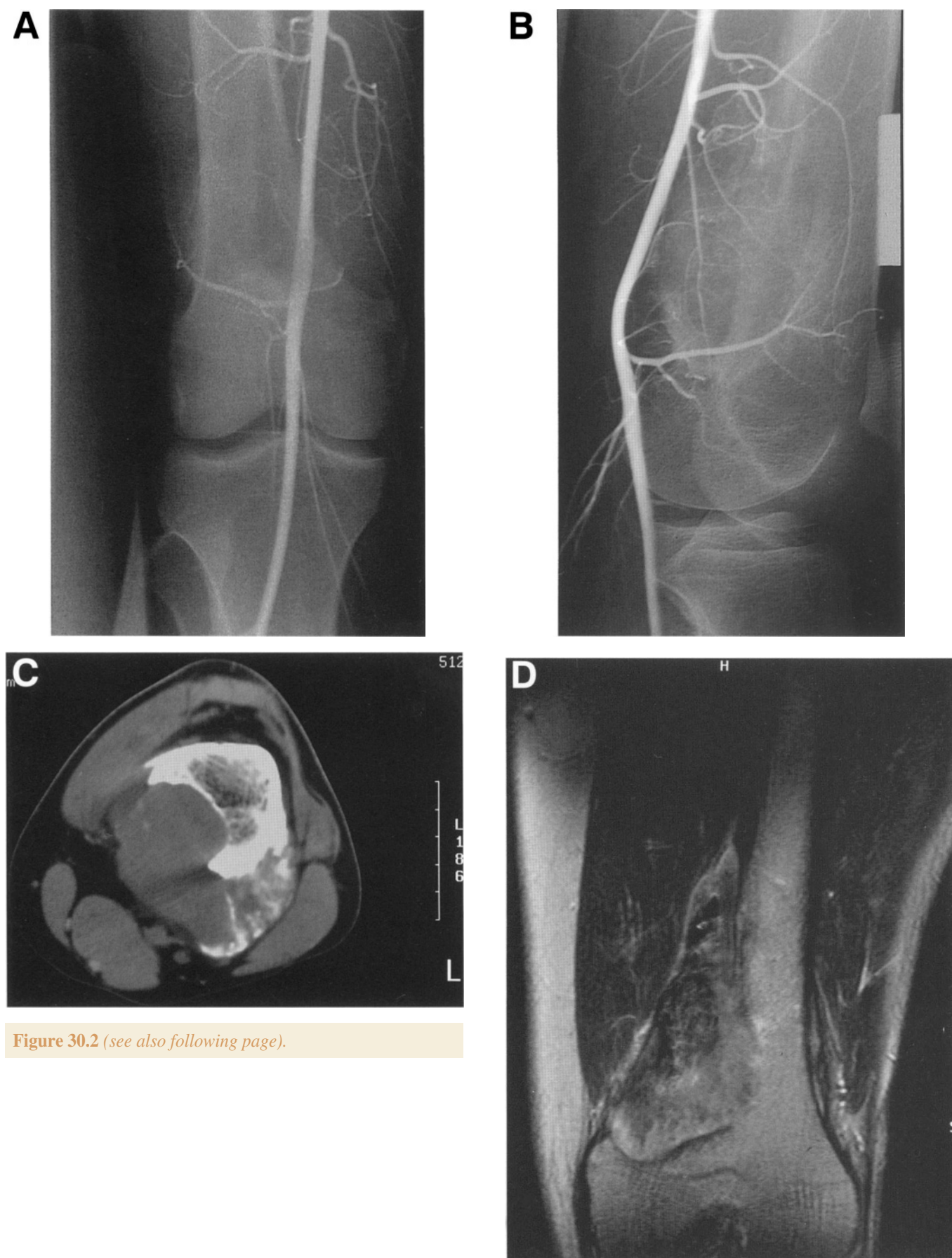


Figure 30.2 (see also following page).



Figure 30.2 (previous page and left) Preoperative evaluation (local staging) prior to surgery. Preoperative imaging studies are essential to determine the extent of surgical resection and to permit adequate surgical resections with negative margins. Routinely angiography, CT, and MRI are utilized. (A,B) Anteroposterior and lateral angiograms of the distal femoral osteosarcoma following induction treatment. Note that there is minimal vascularity to the tumor that indicates a good tumor response to the chemotherapy regimen; that is, a high percentage of tumor necrosis. The popliteal artery is displaced posteriorly and may require a vascular graft depending upon the margins of the adventitia at the time of exploration. (C) Axial CT demonstrating a large posterior component without involvement of the knee joint anteriorly and with some ossification of the tumor on the medial aspect. CT is often utilized with MRI in order to determine the intra- and extraosseous extent of the tumor. (D,E) Coronal and axial MRI views of the same tumor. The coronal view shows the soft-tissue extent and the proximal extent within the marrow. The axial view shows the tumor extent posteriorly that corresponds well with the CT. The MRI is the most reliable study to determine intraosseous extension that permits accurate osteotomy of the femur. CT scans and MRIs are considered complementary examinations when evaluating bony tumors. Additional information is often obtained from each study.

All patients should be considered candidates for limb-sparing procedures unless a surgical oncologist familiar with these procedures feels that a non-amputative option has little chance of success. The final surgical decision is made only after the last cycle of induction chemotherapy, at which time all the staging studies are repeated and re-evaluated.

Bone Scans

Bone scintigraphy is useful in determining intraosseous extension of tumor, and the presence of bony metastases. The area of uptake corresponds to tumor extent and closely estimates the tumor volume. Bone scans are not reliable in detecting extraosseous metastases. Flow and pool studies are helpful in determining tumor vascularity. Comparisons of pre- and postchemotherapy studies can help determine tumor necrosis. A dramatic reduction in uptake correlates with a good response to induction chemotherapy. Caution is advised when interpreting delayed images that may show increased uptake secondary to reactive bone formation despite a good response to chemotherapy.

Computed Tomography

CT allows accurate determination of intraosseous and extraosseous extension of skeletal tumors. It also

accurately depicts the transverse relationship of the tumor and enables the surgeon to detect which portion of the quadriceps muscle is involved and the relationship of the tumor to the popliteal vessels. CT is more accurate than MRI in determining the response to induction chemotherapy. New bone (reparative) formation, tumor ossification, calcification, and fracture healing are best evaluated by CT.

Magnetic Resonance Imaging

MRI allows detailed evaluation of tumor involvement and extent within the marrow of the medullary canal. It also provides details of soft-tissue extension. Of all preoperative studies, MRI is generally the most affected by a prior biopsy or manipulation of the tumor. MRI following a biopsy often overestimates tumor size because of unrelated surgical changes. MRI has not proved reliable in determining tumor necrosis, despite many attempts to evaluate different sequencing techniques with or without gadolinium.

Angiography

Biplanar angiography is essential in determining the relationship of the tumor to popliteal vessels.^{10,11} The angiogram serves as a road map for the surgeon during the operative procedure and permits safe exposure of

the popliteal vessels. Both anterior/posterior and lateral views are required to evaluate the relationship of the vessels to the tumor and the potential plane of resection, and to detect any anatomic distortions or anomalies. The decrease in vascularity of osteosarcomas following neoadjuvant chemotherapy correlates well with tumor necrosis.¹² Pre- and post-induction chemotherapy angiographic studies, taken in combination, provide the most reliable means of assessing tumor necrosis prior to surgery.

Thallium Scans

The use of thallium to evaluate patients with osteosarcoma has become more popular (Figure 30.3). Thalliumchloride is actively taken up by viable tumor cells. A decrease in thallium uptake has been shown to correlate with the tumor-killing effect of chemotherapy. A careful evaluation of all data from the preceding studies allows accurate preoperative determination of tumor extent and permits the surgeon to form a three-dimensional image of the amount of bone and soft tissue to be resected.

BIOPSY

Traditionally, open (incisional) biopsies were performed to obtain tissue for diagnosis. Core needle biopsy, however, usually provides an adequate specimen for diagnosis. Core needle biopsy is less invasive; there is less risk of postbiopsy hematoma, infection, and fracture. Additionally, chemotherapy can be initiated without having to wait for a wound to heal. If it proves to be inadequate, a small incisional biopsy is performed. A medial biopsy is preferred if an option exists. Fine-needle aspirations (FNA) are not recommended. Today, most biopsies are performed under CT guidance or fluoroscopy. Multiple cores can be obtained during a single procedure, through the same puncture site.

It is crucial that the biopsy site be in line with that of the anticipated incision for the definitive procedure. Extreme care should be taken not to contaminate potential tissue planes or flaps that would compromise the management of the lesion. To minimize contamination, a needle biopsy of soft-tissue masses or of extraosseous components should be attempted prior to an incisional biopsy. Radiographs should be obtained to document

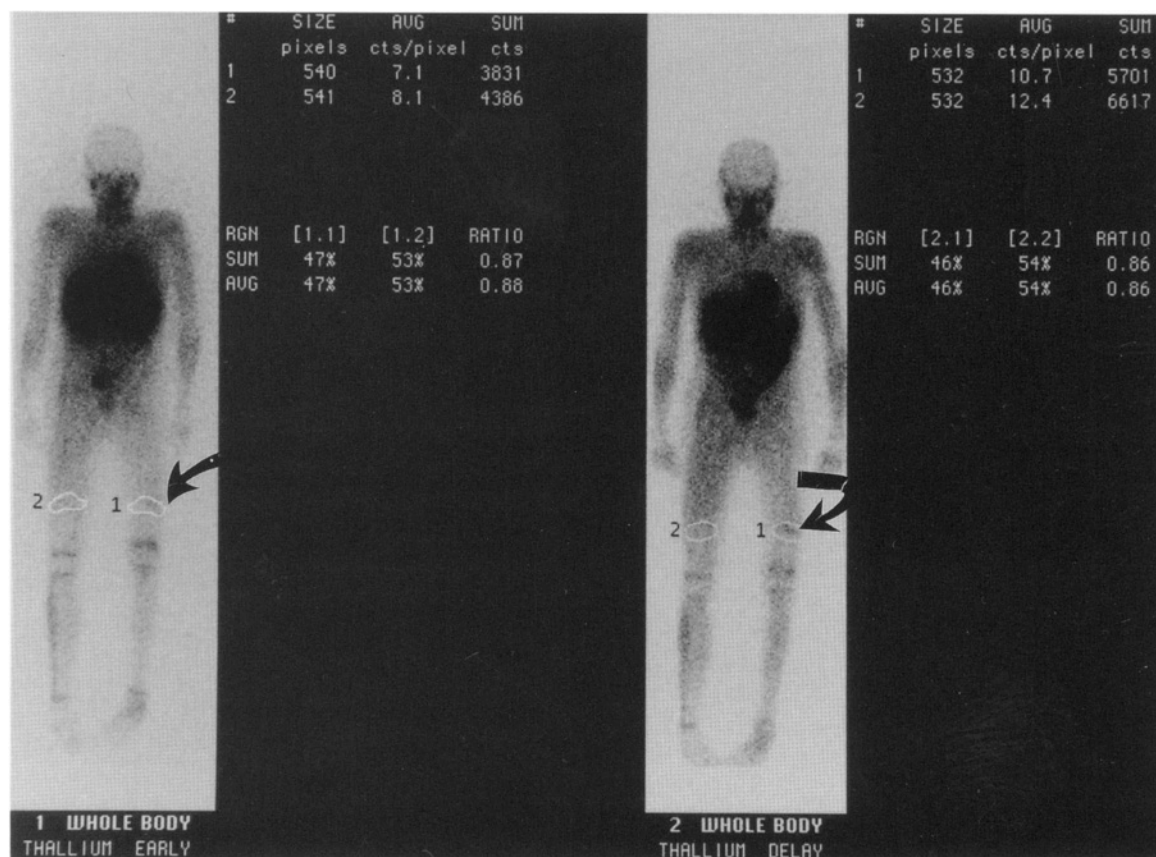


Figure 30.3 Thallium scan (early and late) post-induction chemotherapy. The scan compares the affected side to the normal extremity. Note there is minimal difference in uptake, indicating a good response to chemotherapy. This patient has 100% tumor necrosis.

the position of the needle or the trocar. Care should be taken to avoid contamination of the knee joint, sartorial canal, popliteal space, and rectus femoris muscle.

Regardless of the biopsy technique utilized, tumor cells will contaminate all tissue planes and compartments traversed. All biopsy sites must therefore be removed en-bloc when the tumor is resected.

CONTRAINDICATIONS FOR LIMB-SPARING SURGERY

The contraindications of limb-sparing surgery are as follows:^{3–5,9}

Major Neurovascular Involvement

Major neurovascular involvement, specifically of the popliteal vessels, is usually a contraindication to a limb-sparing procedure. Vascular involvement in itself, however, does not negate a limb-sparing procedure. A vascular graft can replace the popliteal vessels.

Pathologic Fractures

A fracture through a bone affected by a tumor spreads tumor cells via the hematoma beyond limits that can be accurately determined. The risk of local recurrence increases following a pathologic fracture and makes a resection more difficult. There has been increasing experience with limb-sparing surgery in patients with a fracture that heals following induction chemotherapy. In general, if plain radiography and CT show good fracture healing with reossification of the tumor, a limb-sparing resection can be safely performed.

Inappropriate Biopsy Sites

An inappropriate or poorly planned biopsy jeopardizes local tumor control by contaminating normal tissue planes and compartments.

Infection

Implantation of a metallic device or an allograft in an infected area is contraindicated. Adjuvant chemotherapy cannot be administered in the presence of sepsis. This contraindication can ultimately compromise survival. If an infection occurs following a limb-sparing procedure, an amputation is often required in order to be able to give high-dose chemotherapy safely.

Immature Skeletal Age

In the lower extremity the predicted leg-length discrepancy (when the patient has achieved adult stature)

should not be greater than 6–8 cm. Upper-extremity reconstruction is independent of skeletal maturity. An expandable prosthesis or a rotation plasty can be utilized in a young child.^{13,14}

Extensive Muscle Involvement

Enough muscle must remain to reconstruct a functional extremity. In the author's experience the presence of a single contraindication may not dictate an amputation; however, resection is inadvisable in the presence of two or more contraindications.

SURGICAL GUIDELINES

Surgical guidelines for limb-sparing surgery, as practiced by the author, are as follows (Figure 30.5):

1. The major neurovascular bundle (popliteal vessels) must be free of tumor.
2. The resection of the affected bone should leave a wide margin and a normal muscle cuff (i.e. 1–2 cm) in all directions.
3. All previous biopsy sites and all potentially contaminated tissues should be removed en-bloc. All needle biopsy tracts must be removed.
4. To avoid intraosseous tumor extension, bone should be resected 3–5 cm beyond abnormal uptake, as determined by preoperative studies.
5. The adjacent joint and joint capsule should be resected. Adequate motor reconstruction must be accomplished by regional muscle transfers. The type of transfer depends on functional requirements.
6. Adequate soft-tissue coverage is needed to decrease the risk of skin flap necrosis and secondary infection. A medial gastrocnemius rotation flap provides excellent coverage of the prosthesis when required.

PRINCIPLES OF SOFT-TISSUE RECONSTRUCTION

Clinical experience of the past decade has emphasized the need for careful soft-tissue reconstruction and coverage of the prosthesis in order to optimize the functional outcome; decrease the incidence of post-operative complications, infection, and skin flap necrosis; and provide reliable motor function and stability of the knee joint. The principles of soft-tissue reconstruction are described in the following paragraphs.

Restoration of Motor Power

Portions of the quadriceps muscle are usually resected with the distal femur in order to obtain an adequate margin. It is our practice to utilize primary hamstring transfers to reconstruct portions of the quadriceps

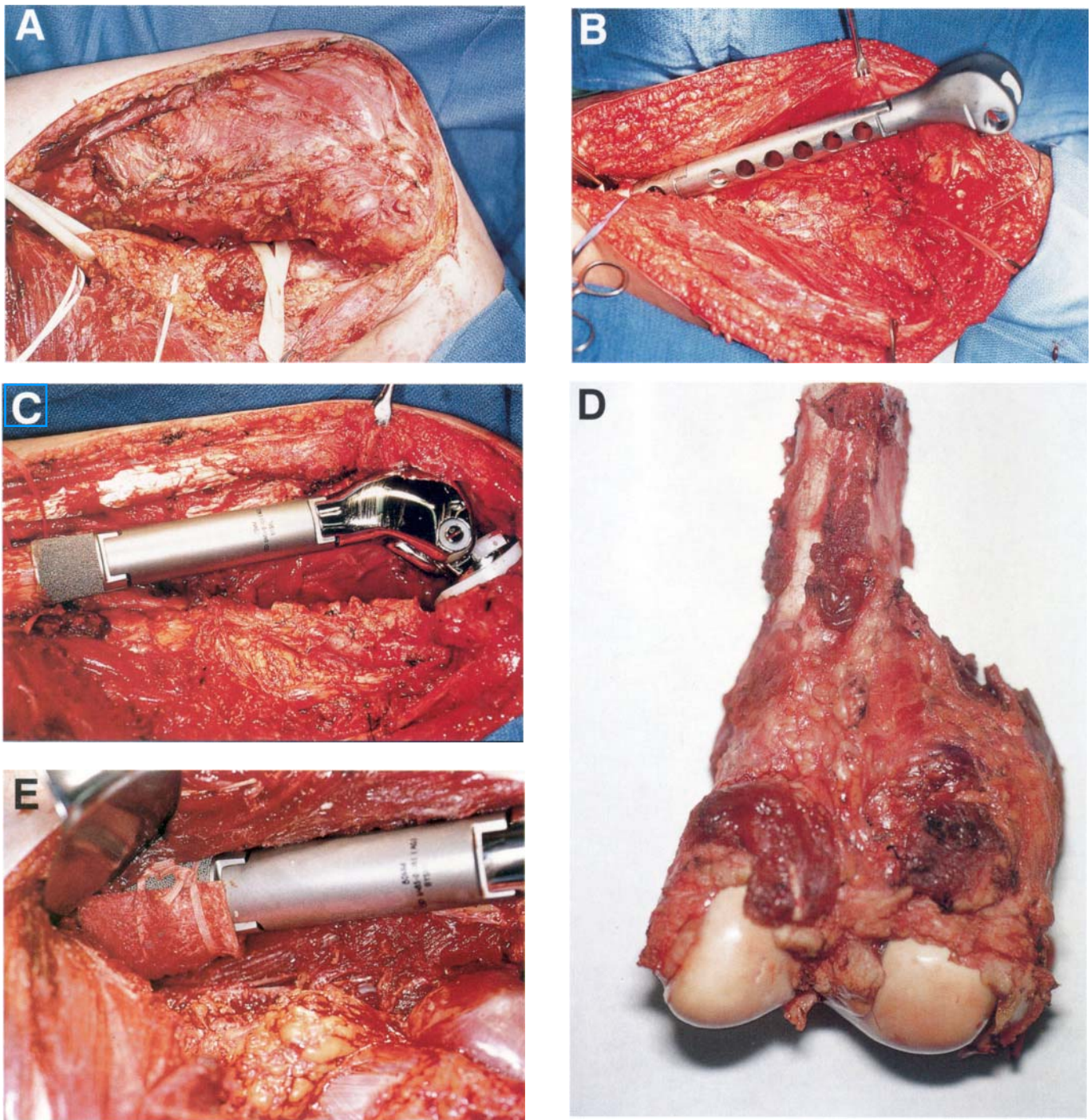


Figure 30.4 (See also following page) Operative photographs of a distal femoral resection for an osteosarcoma with reconstruction using the modular replacement system. (A) Popliteal exposure. Note the Penrose drains are along the popliteal artery distally and at the level of the adductor hiatus proximally. The initial step in resection is exposure of the popliteal vessels and ligation of the geniculate arteries. This permits resection of the distal femur intra-articularly without any surgical complications. (B) Trial distal femoral prosthesis in place. (C) Distal femoral prosthesis in place. (D) Gross specimen of distal femoral tumor. *Note:* muscle surrounds the entire extraosseous component. (E) Close-up of bone graft held with Dacron tape along femur-prosthesis seat (porous coated) for extracortical fixation. (F) Lateral view. (G) Anterior-posterior view. Postoperative radiograph of a typical distal femoral reconstruction utilizing the Modular Replacement System (Howmedica, Inc.). The original design of the Modular Replacement System required cementation of both the femoral and tibial components. The second-generation MRS will permit a choice of stems to permit press fit fixation or cementation.

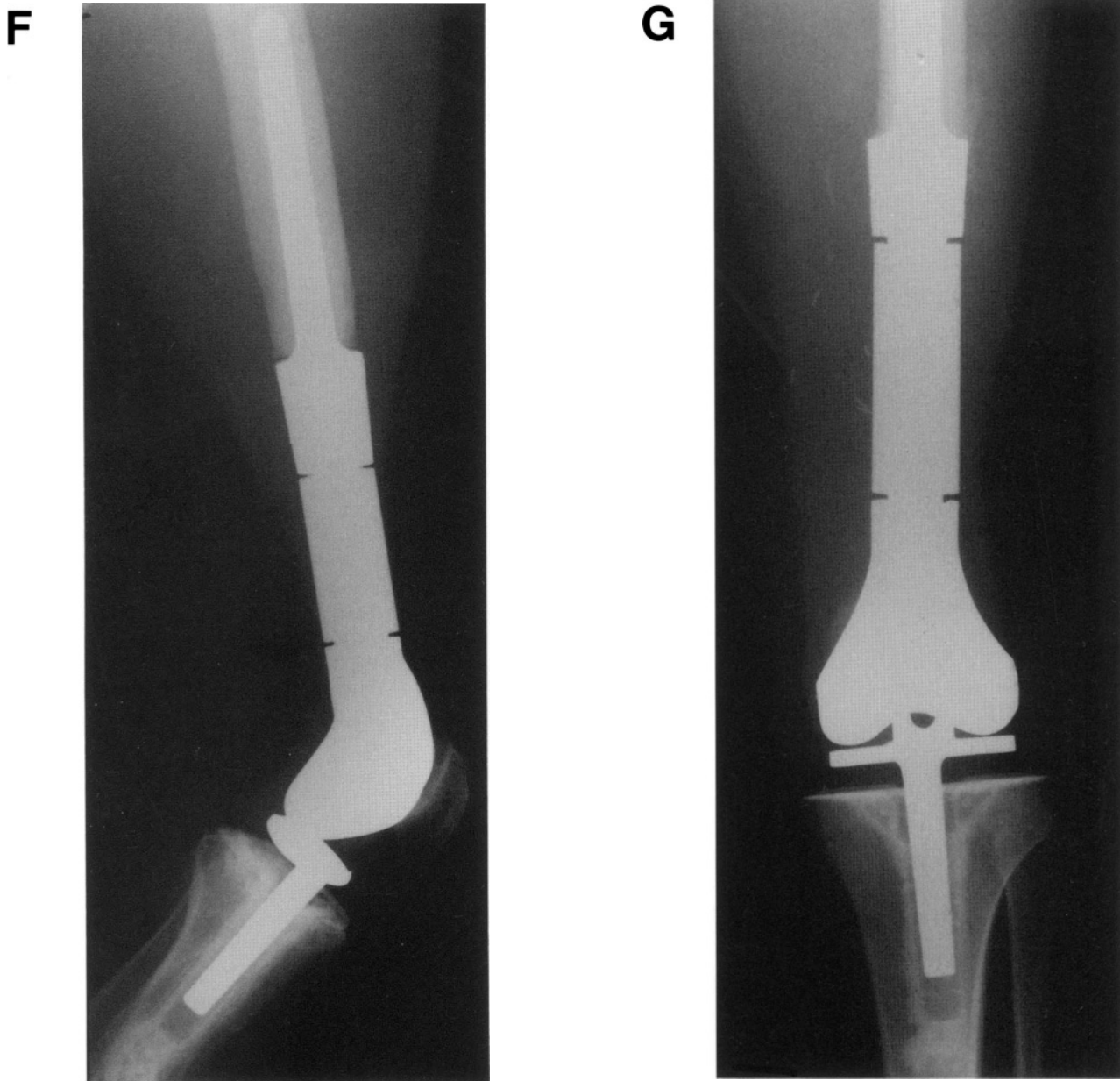


Figure 30.4 F,G

muscles that have been resected. The biceps femoris is an excellent muscle for transfer to the anterior aspect of the knee for both coverage and restoration of loss of the vastus lateralis muscle. The sartorius muscle, which is innervated by the femoral nerve, is an excellent muscle to transfer on the medial aspect of the prosthesis to restore some function lost when the vastus medialis muscle has been resected.

In addition, these transfers are important in stabilizing the patella following resection. Patellar realignment and stabilization is an important component of limb-sparing surgery similar to total knee replacement for osteoarthritis.

Soft-tissue Coverage of the Prosthesis

It is essential to cover the prosthesis with normal muscle. The experience of the 1970s and 1980s showed that a prosthesis or allograft in the subcutaneous position has a relatively high infection rate because of wound flap necrosis. The medial gastrocnemius muscle is the "workhorse" for soft-tissue reconstruction around the knee joint. It is routinely used to cover the knee joint and prosthesis as well as to reconstruct the soft tissue of the medial aspect of the knee. The transfer of this muscle is based on the medial sural artery, which is always retained following popliteal exploration. This muscle



Figure 30.5 Gross specimen of a low- to intermediate-grade osteosarcoma. Note there is a small soft-tissue component. This was one of the first limb-sparing resections performed with a custom prosthesis in 1982. The prosthesis has survived 17 years.

can be transferred transversely to cover the joint or rotated proximally to cover approximately 20 cm of an exposed medial prosthesis. The thick anterior and posterior fascia are routinely removed from the gastrocnemius muscle to permit skin grafting if necessary.

Stability

The prosthesis is inherently stable. Although it is not necessary to reconstruct any ligaments with the Modular Replacement System (MRS), increased strength and stability are necessary to ensure an optimal functioning extremity. Therefore, the above muscle transfers are required to cover and stabilize the prosthesis as well to provide rotational stability in the presence of the rotating hinge mechanism.

Technique of Medial Gastrocnemius Transfer

The technique of medial gastrocnemius transfer was described by Malawer and Price.¹⁵ According to this procedure the medial gastrocnemius muscle is dissected free of its tendinous and midline insertions in the calf following cementation of the prosthesis. It may then be rotated transversely or proximally, depending on the area to be covered. On most occasions the skin can be closed directly over the transferred muscle, but if there is any skin tension or swelling, the skin flaps are sutured directly to the muscle transfer and the remaining defect is closed with a split-thickness skin graft onto the muscle directly at the time of surgery.

It is important to note that the medial gastrocnemius muscle is fed by one major branch: the medial sural

artery off of the popliteal artery. The origin of this branch is below the knee joint line. At the time of popliteal exploration and dissection, it is essential to preserve this branch and not mistake it for a geniculate vessel. The lateral gastrocnemius is rarely utilized because it is a much smaller muscle and its arc of rotation is decreased by the peroneal nerve and the fibula.

THE MODULAR REPLACEMENT SYSTEM

The MRS was developed to meet the needs of patients who require reconstruction of large segmental defects of the knee, shoulder, or hip (Figure 30.6). It is also used to reconstruct osteoarticular defects of varying sizes. The system is assembled intraoperatively and eliminates waiting time otherwise needed to create custom-made devices. Another major advantage of the MRS is that it allows for variation in both planned and unexpected necessary intraoperative changes. The MRS also provides a means of strengthening the implant by extracortical fixation.

The MRS consists of articular components, body segments, stem sections, and a set of trial components. The articular components utilize a male/female Morse taper locking mechanism. They are assembled during surgery by impacting them together. The impaction causes the male/female tapers to produce a cold-type lock. The body segments are available in 40 mm lengths with 20 mm increments. The body segments have a diameter of 28 mm. The stem sections have a 40 mm replacement length with tapered 127 mm stem that is available in 11, 13 and 15 mm diameters; their respective seat diameters are 24, 28 and 32 mm, which allows close matching of host bone. There are two types of stems; one for cementation and the other for press fit porous ingrowth. One area of the body of the stem segment is porous-coated. The porous coating offers the option for bone graft and extracortical fixation.^{16,17} The condylar section has a 65 mm replacement length and is available in left or right. The condyle has a built-in 6° offset. The knee component is a standard, rotating, kinematic hinge-knee component. Smaller femoral components have recently become available for use in pediatric patients.

The trial components are replicas of their corresponding implant; however, they have nonlocking trunnions. The articulating trials are satin-finished so that they can easily be distinguished from the prosthesis. The body sections have several large holes drilled through the major diameter that distinguish them from the implant. The stem sections do not have porous coating. All trial articulating components are made of cast vitallium, and all body segments are made of machined stainless steel.

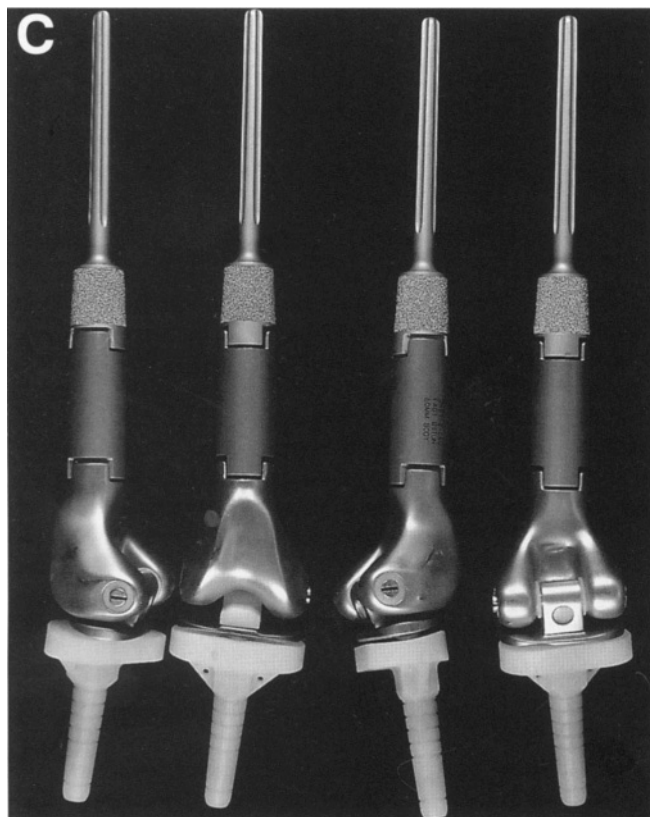
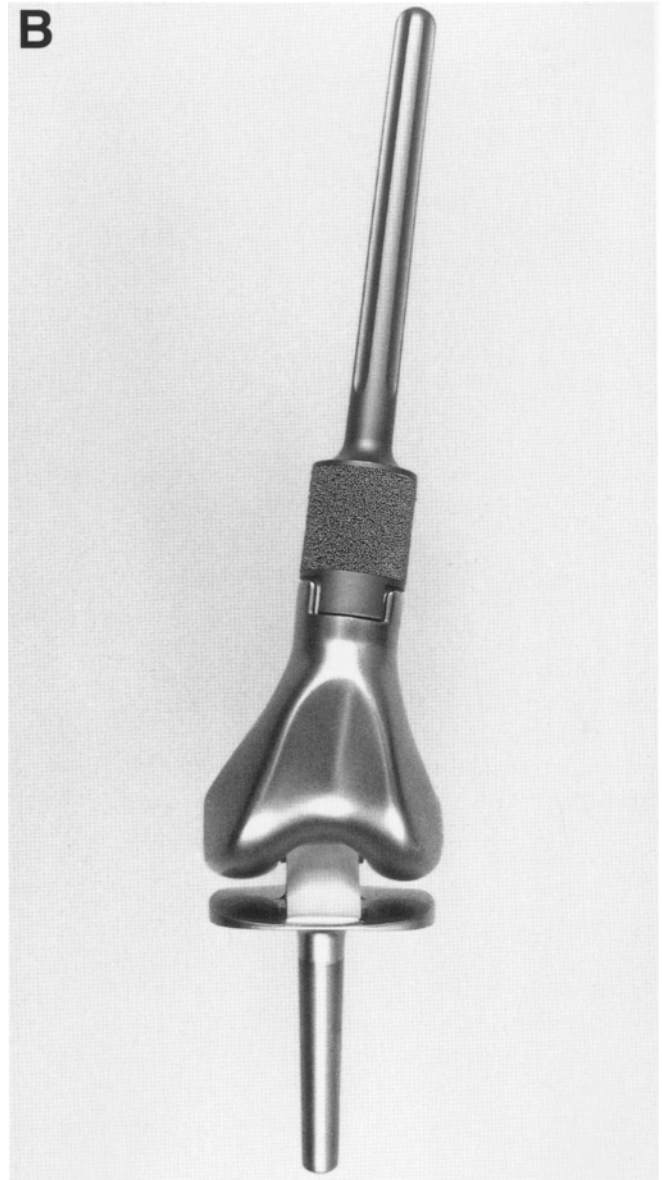


Figure 30.6 (see also following page) Distal femoral modular replacement (Howmedica, Inc.). The most current prosthetic design for replacement of the distal femur is a modular replacement. It consists of a stem of various diameters, a body of various lengths, and a right and a left condyle. These components can be interchanged at the time of surgery, thus avoiding the need for a custom prosthesis in most patients. (A) Composite view of two distal femoral prostheses with and without an intervening body segment. (B) AP view of a distal femoral replacement without a body segment. (C) A composite photograph showing the range of rotation of the distal femur within its polyethylene (tibial) component. The knee joint is a rotating hinge and permits full flexion, extension, and rotation. Control of the extremity is absolutely necessary by the patient's remaining muscles, which may necessitate muscle transfers. (D) Composite photograph showing the range of knee flexion of the tibial component on the modular distal femoral prosthesis.

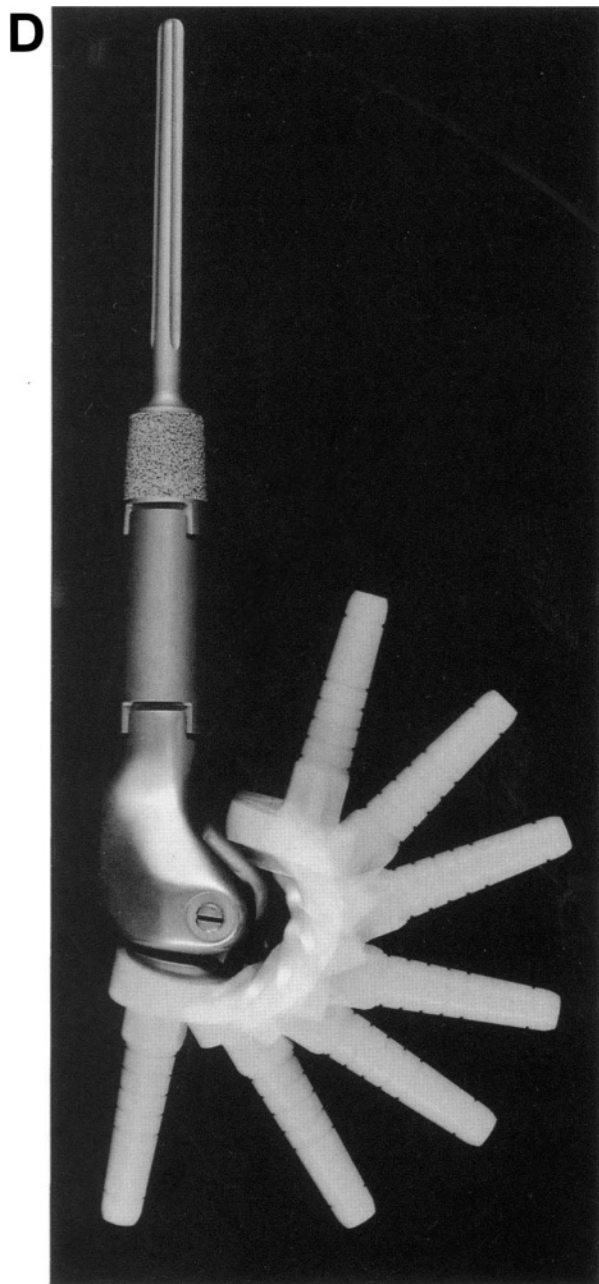


Figure 30.6 D

INTRAMEDULLARY REAMERS

Intramedullary facing reamers correspond to the diameter of the proximal stem. They are used to plane the seat area of bone for the prosthesis. The cutting flutes re-create in bone the radius at the stem/seat junction. The reamers are available in 11, 13 and 15 mm diameters, corresponding to the seat diameters for the femoral system.

Prosthetic Survival Analysis and Results

Major advances have been made in the design and quality of the distal femoral prosthesis, specifically the MRS (Howmedica, Inc., Rutherford, NJ). Henshaw *et al.*¹⁸ have reported the estimated 10-year survival rate associated with use of the distal femoral prosthesis to be 91%. ("Survival" meant the prosthesis did not require removal) (Figure 30.7). No mechanical failures of the prosthesis, taper dissociations, or stem breakage occurred. The incidence of polyethylene failure was less than 10% and usually was a result of failure of the polyethylene bushings. Bushing failure is best detected by a varus and valgus stress test. Bushing failure was rarely seen before 7 years. Failure of the tibial component was rare.

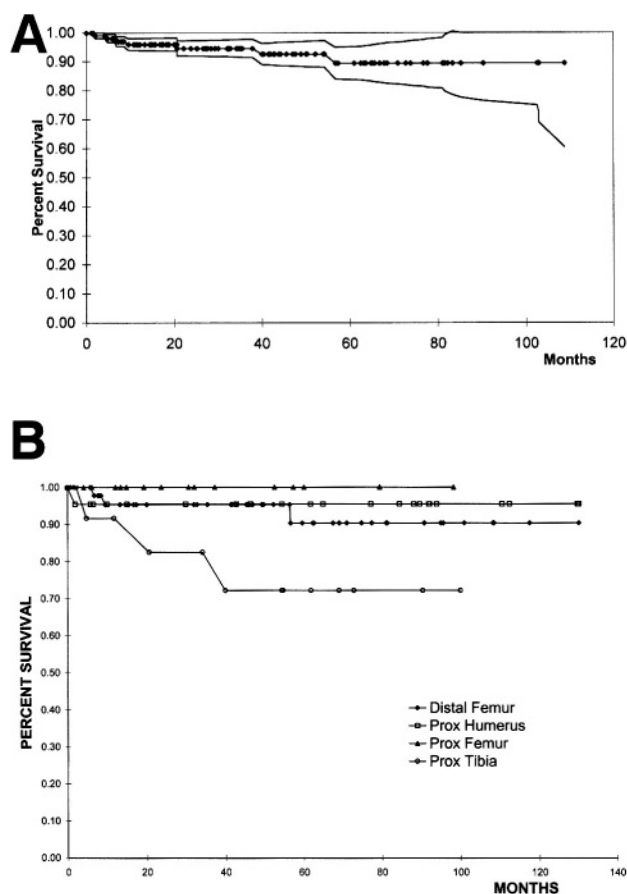


Figure 30.7 (A) Kaplan-Meier analysis of 105 patients treated with a modular replacement prosthesis; 95% of all prostheses were in place at 100 months. (B) Kaplan-Meier analysis of prosthetic replacement by anatomic site. The distal femoral replacements had an overall 91% survival rate at 120 months (10 years).

Functional Evaluation

Eighty percent of patients with distal femoral resections and reconstructions with prosthetic replacements have excellent functional results, and 20% have good results. Range of motion is from 0 to 120 degrees (Figure 30.8). Very few patients demonstrate poor results. Most patients enjoy a normal lifestyle, with limitations only on running and some contact sports.

Postoperative Management

After surgery, postoperative care is as follows:

1. The extremity is kept elevated for 3–5 days. This prevents edema, which may delay wound healing.
2. Continuous suction is required for 3–4 days to avoid fluid collection. This operative procedure involves a large dead space. A 28-gauge chest tube connected to 20 cm of suction is used.
3. Routine perioperative antibiotics are continued until the drainage tubes are removed.
4. Isometric exercises are started the first postoperative day. Knee flexion is generally not permitted until the wound is healed and there is adequate muscle control.
5. Muscle control is essential to prevent rotation of the prosthesis in the early postoperative period. This is a unique consideration associated with this procedure. A knee immobilizer or posterior splint is required.
6. Epineural marcaine catheters inserted into the sciatic nerve are recommended. A continuous infusion of 4–8 ml of 0.25% marcaine is continued for 3–4 days and offers excellent pain relief (Figure 30.9).

PALLIATIVE RESECTIONS OF THE DISTAL FEMUR

A rare but increasingly common indication for distal femoral resection of a high-grade sarcoma, especially an osteosarcoma, is palliation in the face of progressive local and systemic disease. The aims of palliative surgery are to avoid the complications associated with tumor progression, to permit the patient to continue ambulation and function at a fair quality of life, and to control pain. Amputation or limb-sparing resection can accomplish all three aims.

Osteosarcomas that progress locally may present the following clinical findings:

1. hemorrhage into the tumor with significant blood loss;
2. secondary infection; or
3. tumor fungation with secondary infection and bleeding.

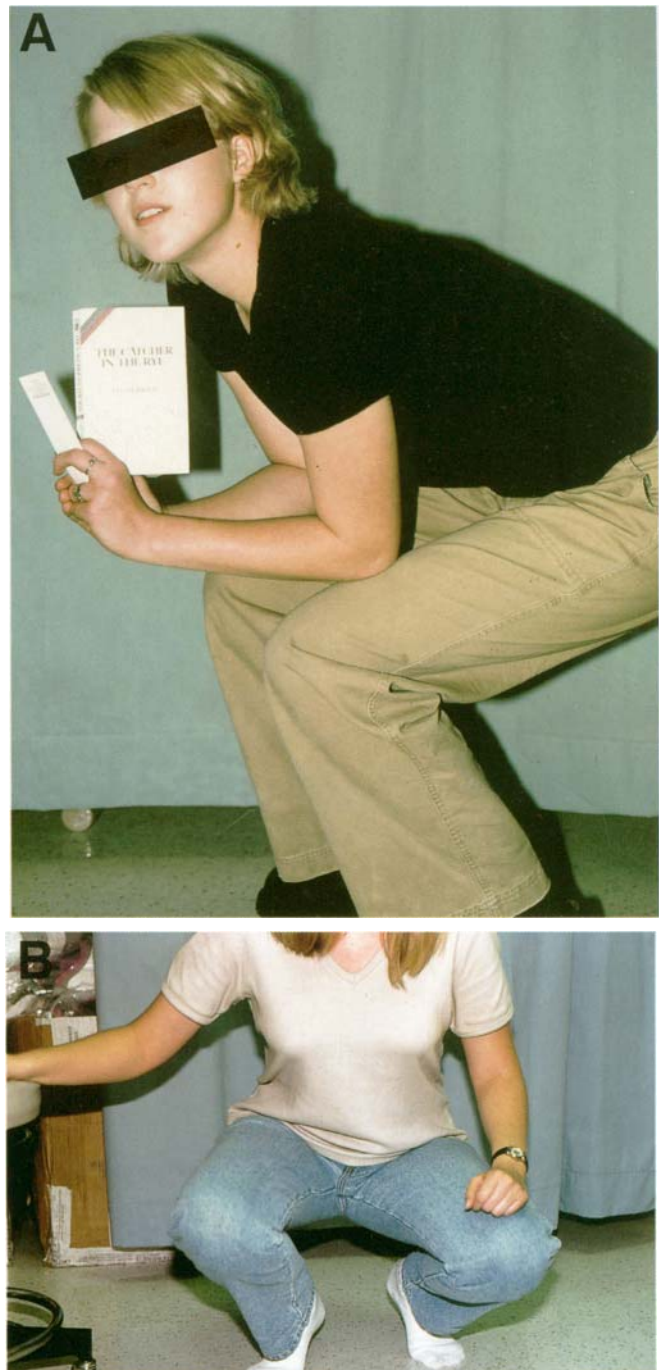


Figure 30.8 Two patients following distal femoral resection and replacement with a modular distal femoral prosthesis showing excellent knee flexion. This is a typical result following distal femoral endoprosthetic replacement. (A) Two years following surgery. (B) Three years following surgery.

This scenario has been seen recently in two specific clinical situations: a patient with multicentric

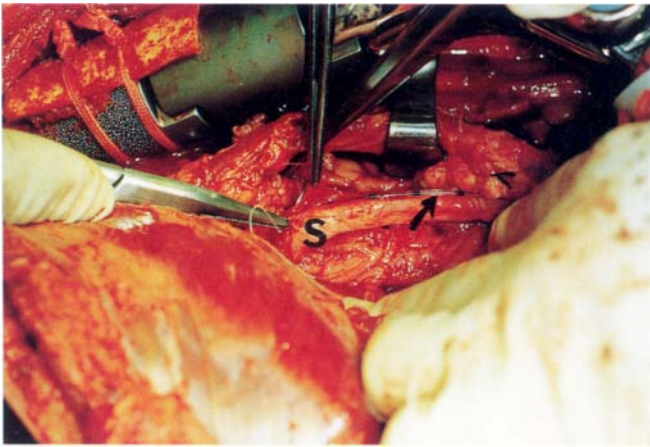


Figure 30.9 Placement of an epineural catheter into the sciatic nerve following segmental resection of the distal femur and replacement with a modular prosthesis. The catheter is shown being sutured into the nerve sheath (catheter, arrows). A continuous marcaine infusion of the major nerves (following a limb-sparing resection) has been utilized by this author for over 10 years. It has been shown to reduce the postoperative use of narcotics by approximately 80% (large arrow, sciatic nerve; small arrow, marcaine epineural catheter). The catheter is brought out of the skin through a separate stab wound. Marcaine (0.25%) is infused at a rate of 4–8 ml/h. This provides excellent pain relief.

osteosarcoma treated with chemotherapy with minimal hope of cure; and a patient who presents with unresectable pulmonary disease treated solely with chemotherapy. Virtually all these patients die from the disease, and surgery for the primary tumor has therefore often been delayed. The large primary site almost always continues to grow, despite chemotherapy, and often progresses to the point where an amputation becomes necessary. The surgeon and the medical oncologist must determine whether the tumor is progressing and should be treated surgically before the inevitable tumor fungation, infection, sepsis, hemorrhage, and chronic pain occur. A relatively early resection is recommended, despite the fact that there is metastatic disease and multicentric disease. This decision to proceed with surgery is not simple; however, surgery does offer the patient an alternative to additional chemotherapy, radiation, and amputation.

The guidelines and the staging studies prior to a palliative resection are generally similar to those that precede a primary resection, with the following modifications:

1. A marginal excision (around the pseudocapsule) with preservation of all function is the goal of surgery.
2. Thick fasciocutaneous flaps with muscle transfers are used if needed to prevent skin necrosis and local infection.
3. Long-term suppressive antibiotics are used if there is an infection.
4. Neurovascular involvement causing severe intractable pain, sensory and motor loss, and lymphedema.
5. Pathological fracture with pain and inability to ambulate.

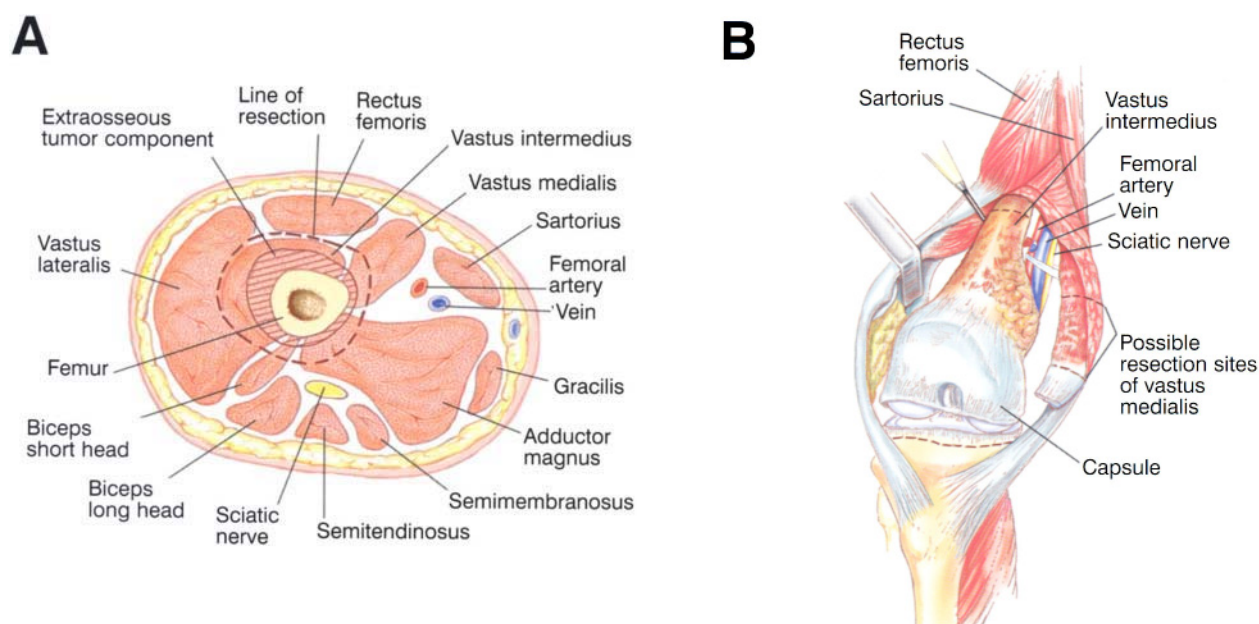


Figure 30.10 (A) Anatomic location of malignancy. Adequate en-bloc resection includes 15–20 cm of the distal femur and proximal tibial plateau and portions of the adjacent quadriceps. (B) An intra-articular resection is usually performed. The surgical planes of resection are shown.

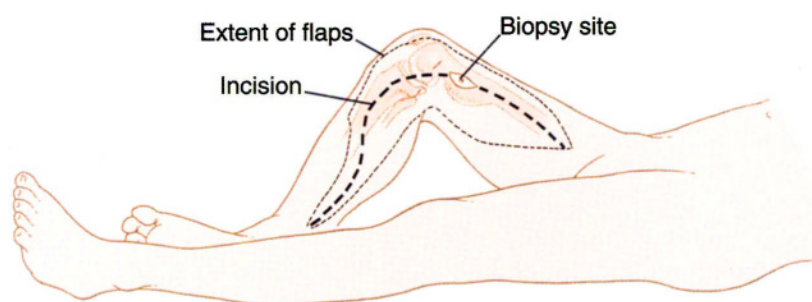


Figure 30.11 Surgical approach and incision. The patient is placed supine on the operating table. A sandbag is placed under the ipsilateral buttock to facilitate taking a bone graft, if necessary. The entire extremity, including the groin and pelvis, is prepped and draped. The groin should always be included to allow for the rare instance in which exposure of the common femoral vessels is required. The pelvis (used for bone graft) is draped separately. A long medial incision begins in the mid thigh, crosses the knee joint along the medial parapatellar area and distal to the tibial tubercle, and passes gently posterior to the inferior border of the pes muscles. The biopsy site is included, with a 1 cm margin in all directions. This approach allows an extensile exposure of the distal one-third to one-half of the femur and knee joint and identification of the important muscle intervals. It allows simple and safe exploration of the sartorial canal, superficial femoral vessels, and popliteal space. It permits distal extension of the incision to develop a medial gastrocnemius muscle transposition for prosthetic coverage. Fasciocutaneous flaps are developed.

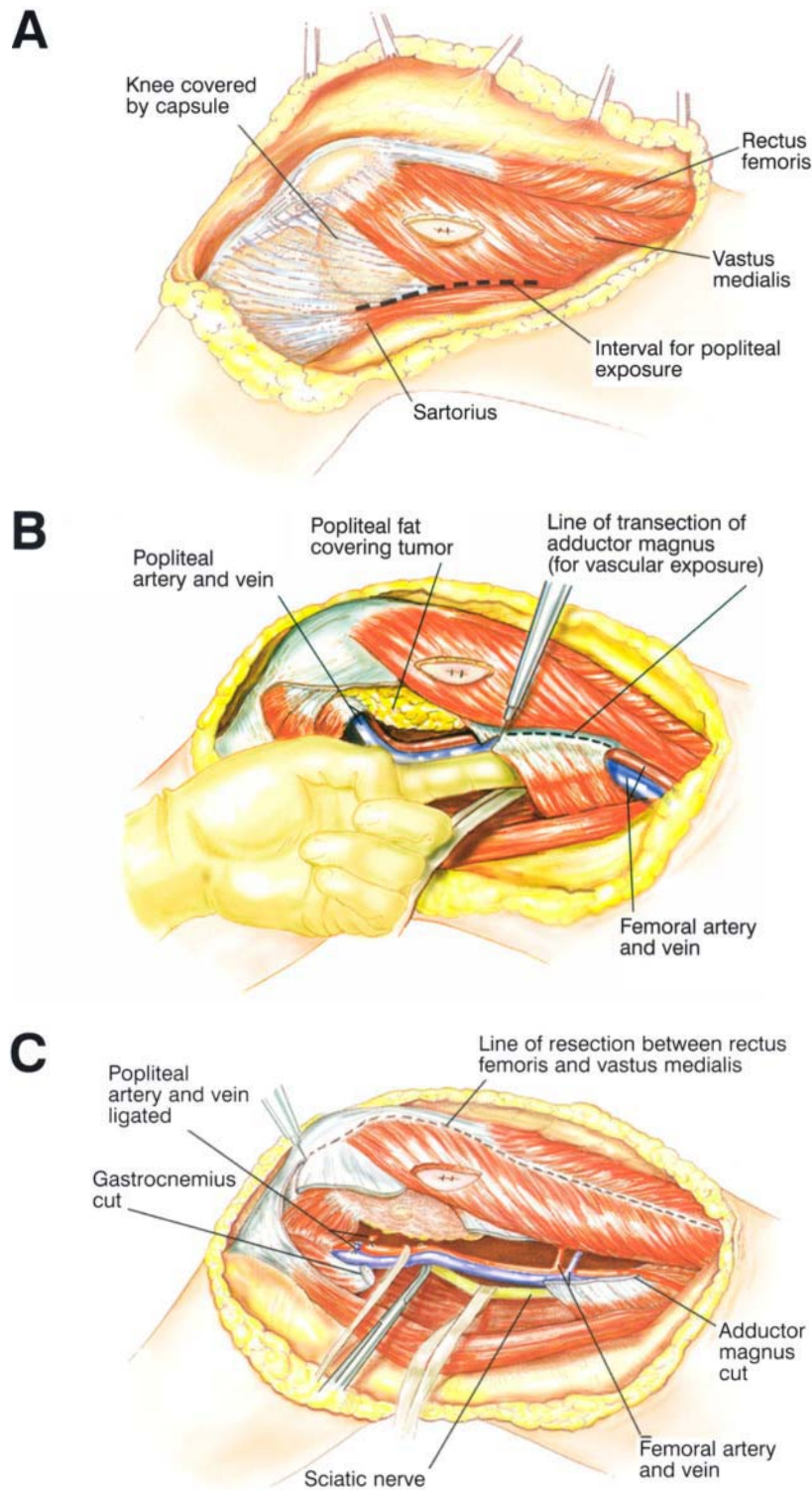


Figure 30.12 (A) Popliteal exploration. Resectability is determined by exploration of the popliteal space and vessels. The popliteal space is approached by detaching or retracting the medial hamstrings. The sartorius is identified. The superior border is opened with the knee in a flexed position. This allows direct entry to the popliteal space and exploration of the popliteal vessels and sciatic nerve. (B) Superficial femoral artery (SFA) exploration. The superficial femoral artery is identified within the sartorial canal. If the resection length is greater than 15 cm, the SFA must be mobilized from the adductors. If this is not done the artery can be inadvertently damaged because of its proximity to the canal as it passes anteriorly to posteriorly. The adductor magnus tendon is released at the foramen to facilitate retraction of the SFA. (C) Posterior exploration. The interval between the popliteal vessels and the posterior femur is developed and explored. The popliteal artery is mobilized, and the geniculate vessels are ligated and transected. If the vessels are free of tumor, resection proceeds. From (Malawer M, Surgical Technique MRS Modular Replacement System. Howmedica, Inc., 1998).

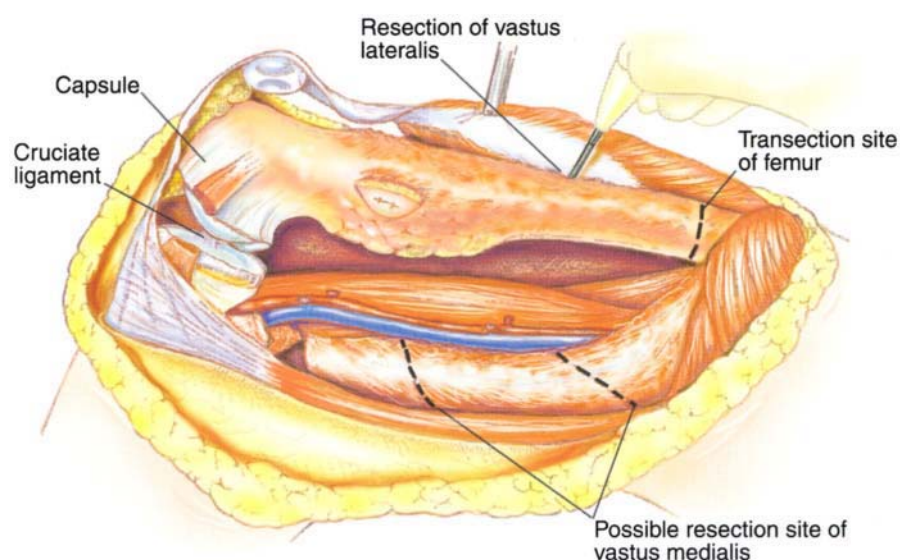


Figure 30.13 Distal femoral resection. The interval between the rectus femoris and vastus medialis muscle is identified and opened, exposing the underlying vastus intermedius muscle. The vastus intermedius must remain intact around the femoral shaft and the extraosseous tumor component. If there is a medial extraosseous component, a cuff of normal muscle must cover it. If necessary, the entire portion of the vastus medialis muscle can be removed en-bloc with the tumor. The entire capsular insertion onto the tibia is completely released. (The stability of the prosthesis is not dependent on the capsule.) The majority of the soft-tissue detachments from the distal femur structures should be performed prior to osteotomy. The remaining muscle attachments to the distal femur, which must be severed, include the medial and lateral intermuscular septa, the short head of the biceps, and both medial and lateral heads of the gastrocnemius muscles.

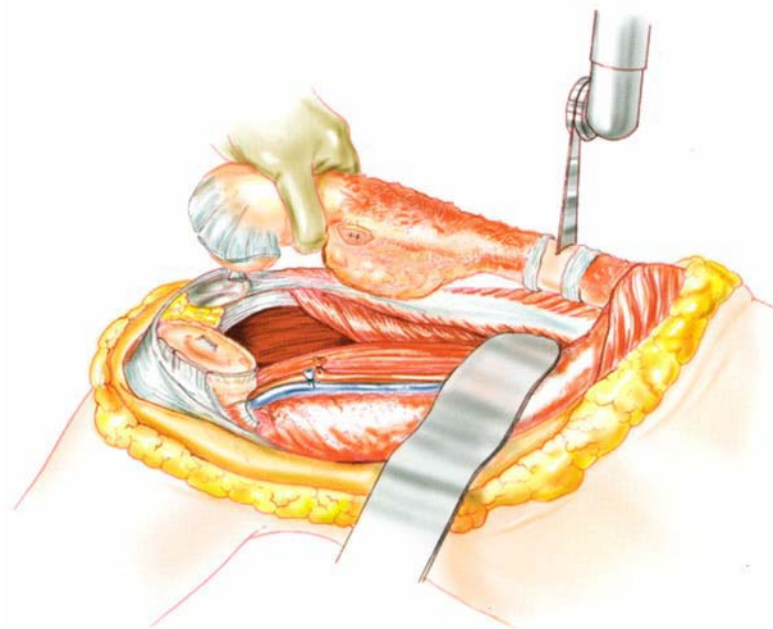


Figure 30.14 Proximal femoral osteotomy. The length of the resection is measured from the medial joint line to the correct area on the femur and then marked. All remaining soft tissue at the level of transection is cleared. The osteotomy is performed after the posterior and medial structures have been protected and retracted; special care is taken to protect the SFA. A frozen section of the bone marrow is performed from the proximal end.

Following the osteotomy, it is helpful to pull the distal end of the femur forward in order to expose the remaining soft-tissue attachments, any remaining fibers of the short head of the biceps, intermuscular septa, and capsular structures are released. The distal femur is then passed off the operative field.

Caution: It is extremely important not to distract the extremity following the resection; one assistant must be assigned to monitor this. The end of the proximal femoral osteotomy should be kept well padded to avoid injuring the popliteal/SFA vessels. The length of the resected specimen should be remeasured following resection.

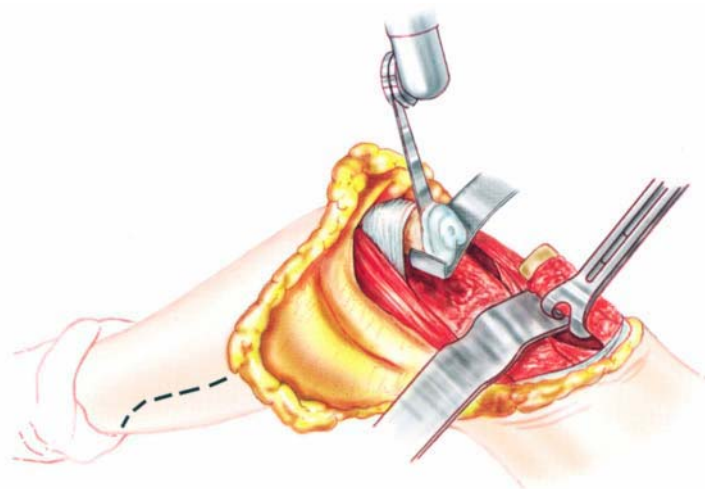


Figure 30.15 Tibial osteotomy and preparation of the femur. The tibial osteotomy is performed in the same manner as the standard knee joint replacement. Approximately 1 cm of bone is removed. The cut should be perpendicular to the long axis of the tibia. Do not discard this bone; it can be utilized for bone graft for the extracortical fixation of the distal femoral component.

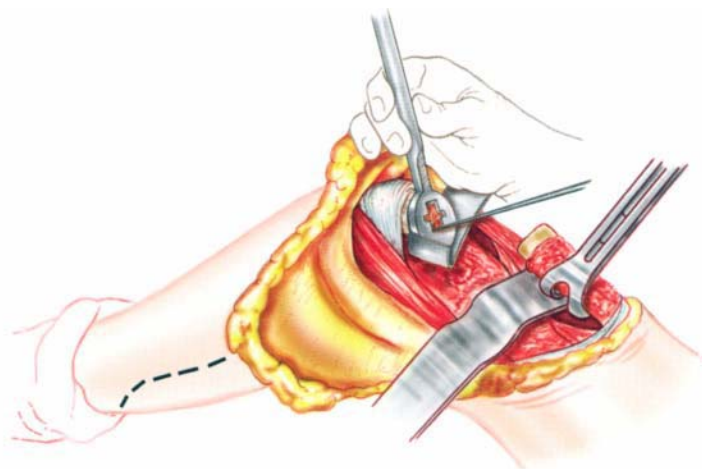


Figure 30.16 Preparation of the proximal tibial canal. The tibial canal is located with a curette. The canal is reamed to the appropriate size, as determined by the preoperative evaluation of the width of the proximal diaphyseal canal. (The stem diameters of the tibial bearing plug component measure 8, 11, 16 and 21 mm; the tibial trial components are not oversized.) The canal is reamed 2 mm larger than the chosen stem diameter to permit an adequate cement mantle. All trial components, with their respective sizes, are marked as trials. The standard tibial template from the Kinematic II (Howmedica, Inc., Rutherford, NJ) rotating hinge is used to outline the rectangular cut for the box portion of the tibial-bearing plug component. The trial tibial-bearing plug component is then impacted with a mallet. The seating of the component must be checked carefully. If necessary, the fit can be adjusted with a small curette or high-speed burr.

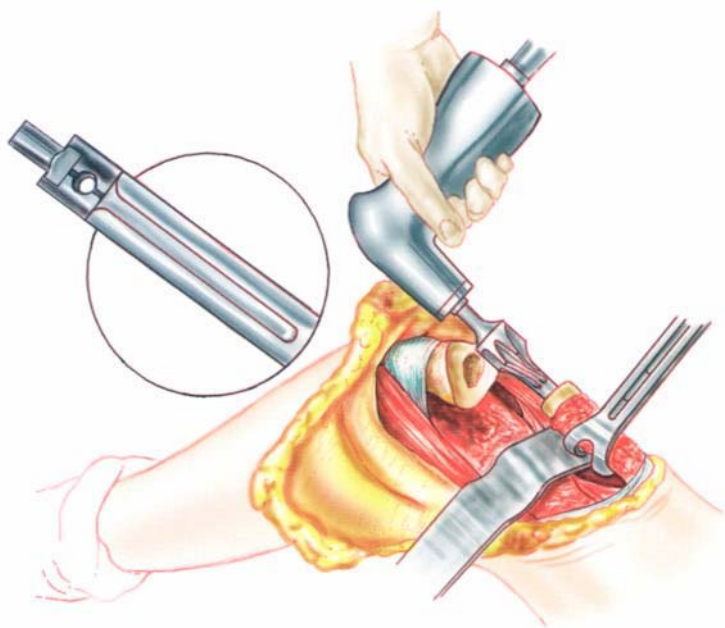


Figure 30.17 Preparation of distal femur. The femur is reamed to 2 mm larger than the stem of the femoral prosthesis. The femoral stems are 11, 13, and 15 mm. The largest stem possible should be used. The corresponding "facing reamer" is used to shape the opening of the femur to permit accurate seating of the prosthesis.

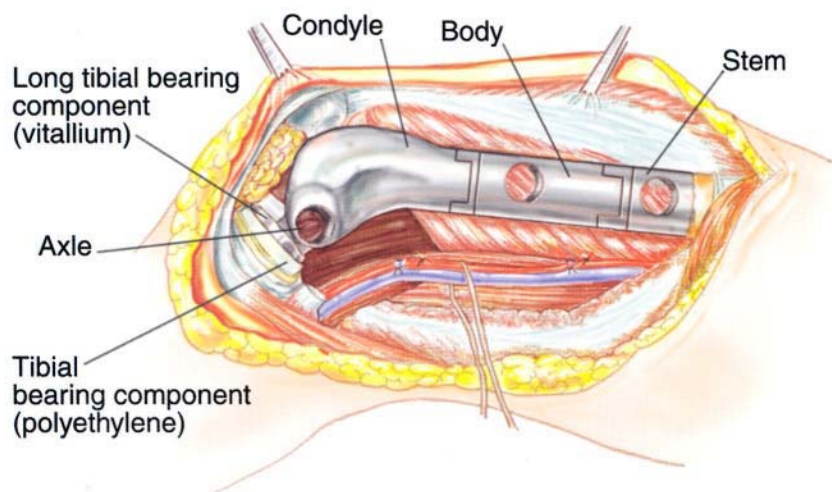


Figure 30.18 Trial reduction with templates. The purpose of the trial reduction is to determine the ease of insertion of the femoral and tibial components prior to cementing, and to determine whether the length of the prosthesis is appropriate.

If the prosthesis is too long, too much tension will be placed upon the neurovascular structures when the knee is extended. In addition, the extensor mechanism will be tight, causing loss of flexion and difficulty in closing the soft tissues. To determine the appropriate length, one must extend the knee and monitor the distal pulse with the trial prosthesis in place. A sterile Doppler can be used to evaluate the posterior tibial and dorsalis pedis pulses. The trial tibial-bearing component is inserted into the tibia and impacted with a mallet. Insert the femoral stem segment into the femur. The femoral stem segment is aligned using the linea aspera as a guide. An imaginary perpendicular line is constructed that passes directly anterior, originating from the linea aspera. The horizontal axis of the prosthesis should be perpendicular to this line. The trial femoral prosthesis is assembled by joining the femoral stem segment with the trial femoral body segment and condylar segment.

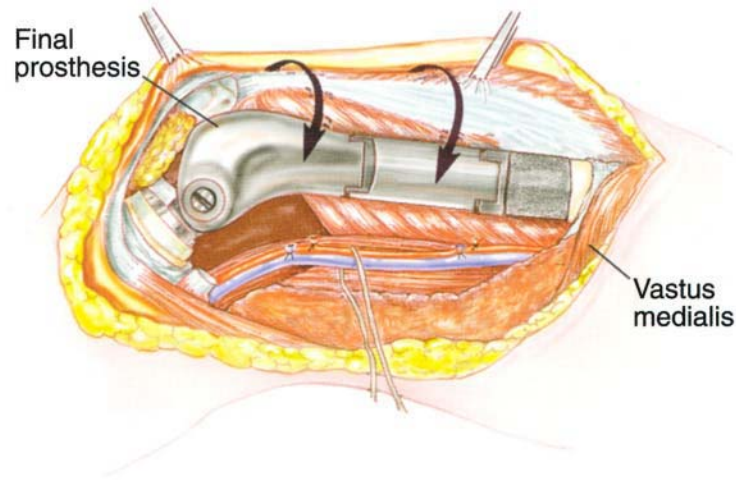


Figure 30.19 Trial articulation. Four parts must be assembled to articulate the femoral and tibial components: standard long tibial bearing (vitallium), an axle, two bushings, and a bumper. Once the prosthesis is articulated, the femoral components are held in one hand to prevent rotation, and extend the legs fully. The femoral vessels are palpated to determine the status of the pulse or evaluate the pulses at the ankle with a sterile Doppler. If the pulse is diminished, the knee is flexed to determine if it increases. This will indicate the need either for modifying the length of the prosthesis or for removing additional bone from the distal femur. The range of motion of the knee with the patella relocated is tested. A full range of motion should be obtained. The surgeon must note whether the capsular mechanism and soft tissues can be easily closed. These factors, taken together, determine the adequacy of the length of the resection.

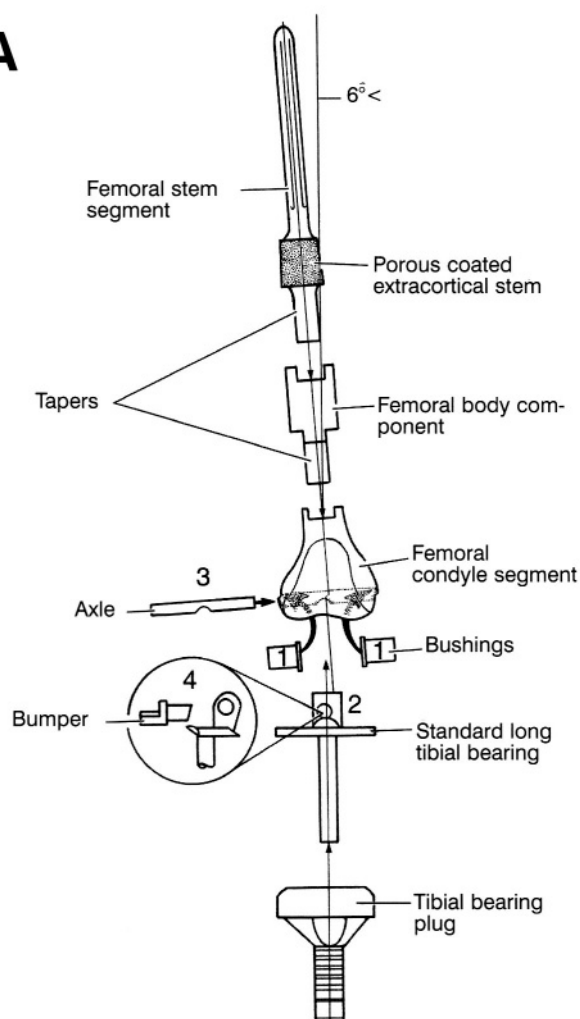
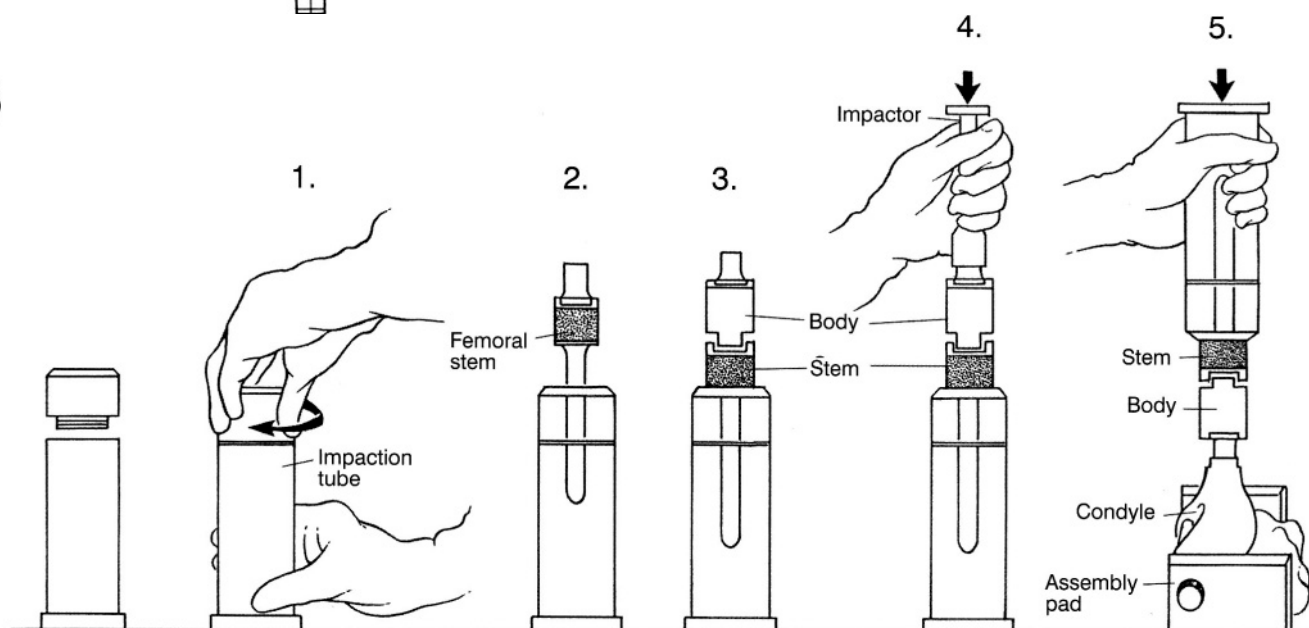
A**B**

Figure 30.20 Assembly of prosthesis. (A) The femoral prosthesis consists of three components: the femoral stem segment, femoral body component, and femoral condyle segment. There are two femoral condyle components: right and left. The correct side and the lengths of all components are checked before assembly. The three instruments necessary for the assembly are the impactation tube, impactor and assembly pad. Before joining any of the tapers, one must make sure that all components are completely dry. (B) The femoral body component and femoral stem segment are assembled first. The femoral stem segment is placed into the impactation tube (1,2) and the femoral body component is mated with it (3). The impactation tool is placed over the taper of the femoral body component (4) and impacted with a swift blow of the heavy mallet.

The femoral condyle component is placed onto the distal end of the femoral body component (5). The entire prosthesis is removed from the impactation tube and placed with the femoral condyles against the assembly pad. The impactation tool is placed over the stem against the base of the prosthesis and impacted with a swift blow. Once the prosthesis is assembled, the tapers should not disengage.

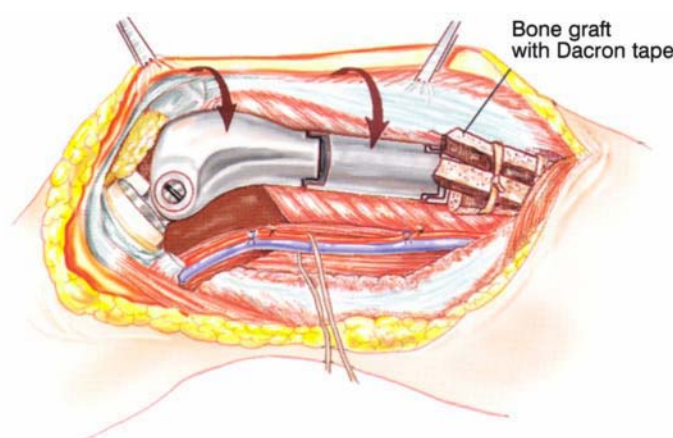


Figure 30.21 Implantation and orientation of the femoral prosthesis. The femoral canal is thoroughly irrigated. A cement plug is placed at the appropriate depth. This depth is checked by inserting the actual prosthesis and verifying complete seating. The femoral canal is again irrigated and dried. The soft tissues, especially those that are near the neurovascular structures, are protected and packed off with wet lap pads. Two packs of PMMA are mixed and injected into the canal to ensure complete filling of the canal. Some PMMA is then placed around the stem of the prosthesis. The femoral prosthesis is oriented with the linea aspera as the guide. This is the only landmark. There is no guide for femoral alignment. The prosthesis is then impacted. Excess cement is removed from around the prosthesis. Care is taken to prevent cement from getting into the porous-coated section. The articulation of the actual prosthesis is identical to that of the trial.

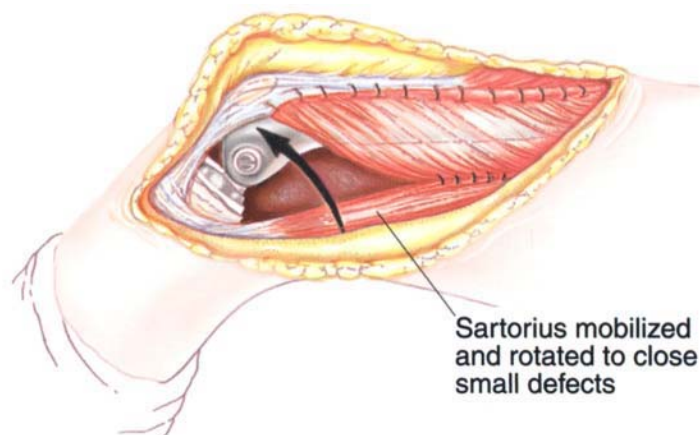


Figure 30.22 Sartorius muscle. It is essential to completely cover the prosthesis with soft tissue. The prosthesis should not be left in a subcutaneous position. The remaining vastus medialis muscle is sutured to the rectus femoris. The sartorius muscle can be mobilized and rotated anteriorly for closure of a small remaining defect. A large defect requires a medial gastrocnemius transfer; a lateral defect is closed with a lateral gastrocnemius transfer.

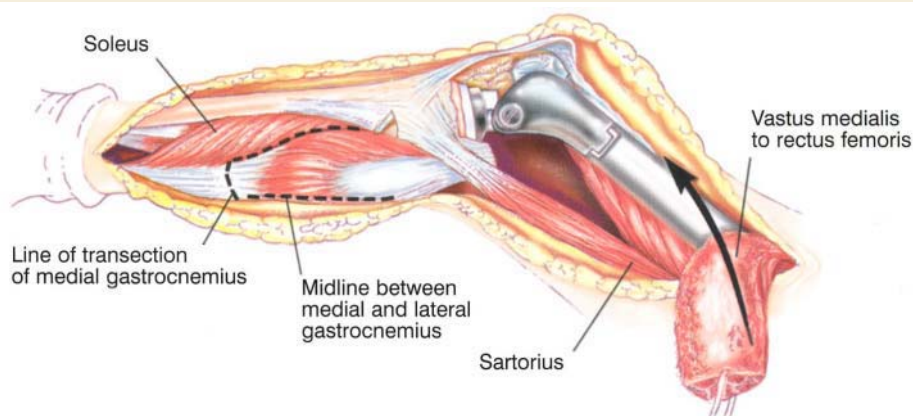


Figure 30.23 Exposure of the medial gastrocnemius. To adequately expose the medial portion of the gastrocnemius muscle, one must: (1) increase the length of the incision distally to the level of the musculotendinous junction; (2) create a posterior-based midline fasciocutaneous flap; (3) expose and open the interval between the medial gastrocnemius muscle and soleus muscle by lifting the medial gastrocnemius muscle by finger dissection. Exposure stops at the midline.

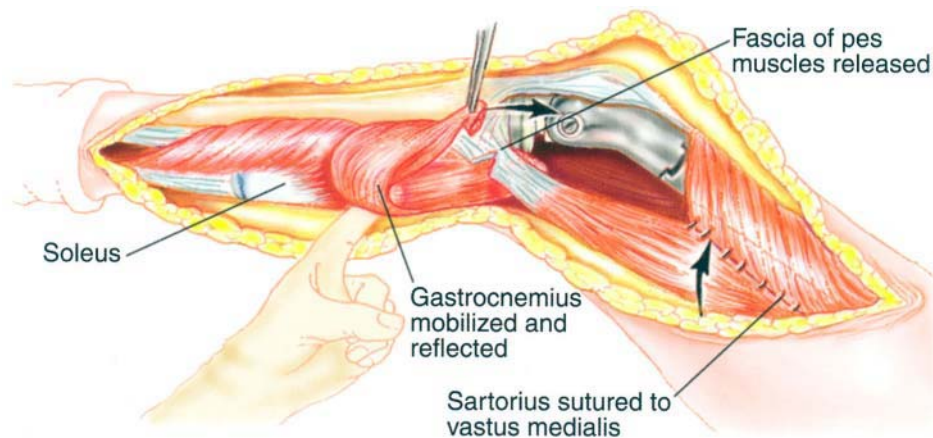


Figure 30.24 Mobilization of medial gastrocnemius muscle. The medial portion of the musculotendinous junction is detached and the two muscle bellies are separated along the midline.

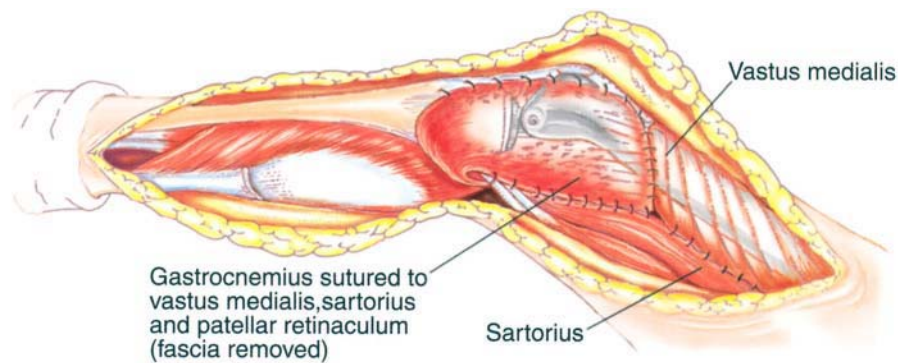


Figure 30.25 Rotation of the muscular flap. Rotate the flap anteriorly over the prosthesis. Occasionally, the fascia of the pes musculature must be released to increase the arc of rotation. The thick anterior and posterior fascia of the medial gastrocnemius is removed in order to spread the muscle over a larger area.

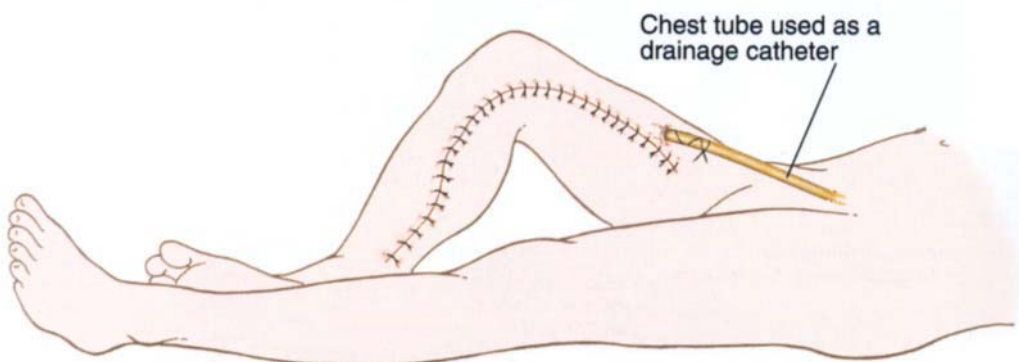


Figure 30.26 Wound closure. A 28-gauge chest tube is attached to Pleurovac suction (20 cm of water). The pulses are checked following wound closure and prior to removing the patient from the table. A knee immobilizer is used.

DISCUSSION

Limb-sparing surgery is now the preferred treatment for the majority of patients with osteosarcomas or other high-grade sarcomas (e.g. malignant fibrous histiocytoma, fibrosarcoma, and malignant giant cell tumors).¹⁻⁸ Almost all low-grade sarcomas of the distal femur, especially parosteal osteosarcoma and chondrosarcoma, can be treated safely with a limb-sparing resection. Careful preoperative planning and patient selection are crucial to a successful outcome. All patients with high-grade bone sarcomas of the distal femur should undergo preoperative CT, MRI, bone scintigraphy, and biplane angiography. All patients should be evaluated for a limb-sparing option prior to proceeding with an amputation.

Preoperative (induction) chemotherapy has changed our indications for patient selection.¹⁹⁻²¹ Approximately three-fourths of patients who would formerly have been considered unresectable were converted to limb-sparing procedures following induction chemotherapy consisting of two cycles of intra-arterial cisplatin and continuous intravenous Adriamycin.^{8,21,22}

This chapter describes prosthetic replacement as the method of reconstruction of a large tumor defect. We assume that a prosthesis such as that described here may have to be revised. The use of improved cement techniques, extracortical fixation, and newer metals such as titanium will, it is hoped, increase the longevity of the prosthesis. Some surgeons favor osteoarticular allografts. In general they are not recommended for patients with high-grade sarcomas requiring adjuvant chemotherapy because of the increased risk of infection, nonunion, fracture, and subsequent delay in receiving chemotherapy. Arthrodesis (fusion) is a reliable procedure that may last the life of the patient.²² Its major drawback is a stiff knee. We prefer arthrodesis only as a limb salvage procedure.

Several considerations can help decrease the complications of limb-sparing procedures. These are as follows:

1. A single medial incision, which allows adequate exposure of most lesions, is recommended.
2. A wide exposure is necessary in order to avoid tumor contamination. Large fasciocutaneous flaps are required.
3. Adequate soft-tissue reconstruction is mandatory in order to avoid wound breakdown. A medial (occasionally, lateral) gastrocnemius transfer is required to cover the prosthesis.
4. Adequate and prolonged postoperative tube drainage of the resection site is needed to decrease secondary wound problems.
5. We recommend the use of a 28-gauge chest tube for 3–5 days.

The MRS is a design that incorporates the advantages of several different features of prosthetic design. It increases the longevity of the prosthesis.¹⁰ The kinematic rotating hinge component, which has been used since 1981, is one of the most effective means of decreasing stress on the stem and ensuring stability.¹⁸ In general, the stem is the most vulnerable site of potential prosthesis loosening and failure. Mechanical stability is required, since all soft-tissue attachments to the knee are usually removed in order to adequately resect the tumor. The hinge component provides stability, and the rotary component permits a large amount of rotation. In comparison with a straight hinge, or earlier knee designs, there is significantly less stress on the bone–cement interface. The MRS mates this design with a modular system that permits immediate availability of prostheses of different sizes. The extracortical porous coating may provide additional bony fixation with the prosthesis, which may further decrease the stress on the stem and permit more physiologic cortical transmission of forces. Soft tissue may also grow into the porous surface thus shielding the bone prosthesis interface from ingress of particulate polyethylene debris.

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Proximal Tibia Resection with Endoprosthetic Reconstruction

Martin Malawer

OVERVIEW

Resection is a limb-sparing option for low-grade bony sarcomas and most high-grade (Stage IIA or IIB) sarcomas (e.g. osteosarcomas) arising from the proximal tibia. In the past, several surgical and technical problems made it impossible to perform limb-sparing surgery for tumors at this site. These problems included anatomic constraints, a difficult surgical approach, inadequate soft-tissue coverage, vascular complications, and the need to reconstruct the patellar/extensor mechanism. Appreciating these challenges, most surgeons recommended above-knee amputation for these lesions.

The limb-sparing technique illustrated in this chapter allows a safe approach to the dissection of popliteal vessels and to the resection and replacement of the proximal one-third to two-thirds of the tibia. Preoperative evaluation of tumor extent requires a detailed understanding of the anatomy and careful evaluation by computed tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy, and biplane angiography. The major contraindications to limb-sparing surgery are a pathologic fracture, neurovascular involvement, or contamination from a poorly positioned biopsy. One-half to two-thirds of the tibia is removed, along with a portion of all muscles inserting on the tibia and the entire popliteus muscle, in combination with an extra-articular resection of the proximal tibiofibular joint. The peroneal nerve is preserved. The surgical options for reconstruction are primary arthrodesis, prosthetic replacement, or allograft replacement. We prefer a prosthetic replacement; allograft replacements have a high rate of infection, fracture, and local tumor recurrence. One key to the success of this procedure is the use of a gastrocnemius muscle transfer to obtain reliable soft-tissue coverage that helps prevent skin flap necrosis and secondary infections, and provides for reliable extensor mechanism reconstruction. Most patients with low-grade sarcomas, and approximately half of those with high-grade sarcomas, of the proximal tibia can be treated by a limb-sparing resection.

INTRODUCTION

The proximal tibia is the second most common site for primary bony sarcomas.¹ Because of several unique surgical problems, and the difficulty of reconstruction, this site is a difficult area in which to perform a safe limb-sparing resection that preserves function. There have been only a few reports of limb-sparing resections for high-grade sarcomas of the proximal tibia.^{2–6} Most surgeons still recommend above-knee amputations even though good results, widespread acceptance, and varied techniques for limb-sparing resections of bony sarcomas (distal femur^{3,7–9} and of the tibia) have been reported for giant-cell tumors and low-grade sarcomas (i.e. chondrosarcomas) (Figure 31.1).^{5,10–12}

The difficulty in performing a successful resection for a high-grade sarcoma of the tibia arises from the local anatomy, rather than from any inherent properties of the tumor. In fact, persons with osteosarcomas of the proximal tibia have higher survival rates than those with tumors of the distal femur.^{13–15} The surgical and technical problems include intimate anatomic relationships, a difficult surgical approach, inadequate soft-tissue coverage, and vascular complications. In addition, unique to an arthroplasty of the proximal tibia is the need to reconstruct the patellar tendon (extensor mechanism). Finally, one must deal with a second adjacent joint, the proximal tibiofibular joint. These difficulties have often led to a high rate of early postoperative complications, foremost among which is failure of reconstruction. The ultimate result was a poor functional outcome and/or secondary amputations.

This chapter describes a technique developed by the senior author during the past 20 years, that permits safe and easy access to the popliteal vessels, resection and replacement of a large segment of the tibia and knee joint, and a method of patellar/extensor mechanism reconstruction and soft-tissue coverage that utilizes a transferred medial gastrocnemius muscle (Figures 31.2 to 31.5). The unique anatomic considerations, as well as the staging studies that are necessary to determine resectability, are emphasized.^{6,16–18}

INDICATIONS

Indications for proximal tibia resections include low-grade bony sarcomas (usually chondrosarcomas), recurrent aggressive benign tumors (especially giant-cell tumors), and carefully selected high-grade sarcomas.^{4,5,11,12} The most common high-grade bony sarcoma is osteosarcoma; malignant fibrous histiocytoma and fibrosarcoma are less common.^{6,16} Round-cell sarcomas (e.g. Ewing's sarcoma of bone) were traditionally treated by radiation combined with chemotherapy.

In recent years Ewing's sarcoma has been treated by induction chemotherapy and resection with a prosthesis replacement; no postoperative radiation is used if margins are negative. Candidates for resection are selected on the basis of a careful evaluation of the local tumor extent, placement of any previous biopsy sites, and the patient's functional demands. The preoperative assessment must include an evaluation of the length of bone resection that would be required (usually not more than one-half to two-thirds of the tibia); the degree of soft-tissue, capsular, and patellar tendon involvement; and the tumor-free status of the popliteal trifurcation (Figures 31.6 and 31.7).

Contraindications to resection include a pathologic fracture, extensive contamination from a poorly positioned biopsy, tumor penetration through the skin, and local sepsis. Relative contraindications include a large posterior extraosseous component and immature skeletal age. Expandable prostheses are used in younger patients in the hope of avoiding future problems related to leg-length discrepancy (Figure 31.5).

UNIQUE ANATOMIC CONSIDERATIONS

Popliteal Trifurcation

Surgical procedures of the popliteal space require extremely careful preoperative planning, beginning with an evaluation of the vascular pattern around the knee. The popliteal artery divides into the anterior tibial artery, the posterior tibial artery, and the peroneal artery at the inferior border of the popliteus muscle. The popliteal trifurcation is actually two bifurcations. The first is found at the place where the anterior tibial artery arises from the popliteal artery, which then continues as the tibioperoneal trunk. The anterior tibial artery is the first branch and arises at the inferior border of the popliteus muscle. The second bifurcation is found where the peroneal artery and the posterior tibial artery arise from the tibioperoneal trunk; thus, the second bifurcation is distal to the anterior tibial takeoff. It is almost always essential to ligate the anterior tibial artery at the time of resection; the other vessels must be identified before ligation. A unique and fortunate occurrence is the popliteus muscle that covers the posterior surface of the tibia, which affords an excellent boundary between posterior soft-tissue extension from the tibia and the popliteal artery and its branches. This is in contrast to the distal femur, in which the posterior aspect is covered only by the popliteal fat.

Tibiofibular Joint

The proximal tibiofibular joint is in close proximity to the posterolateral aspect of the proximal tibia. Histologic

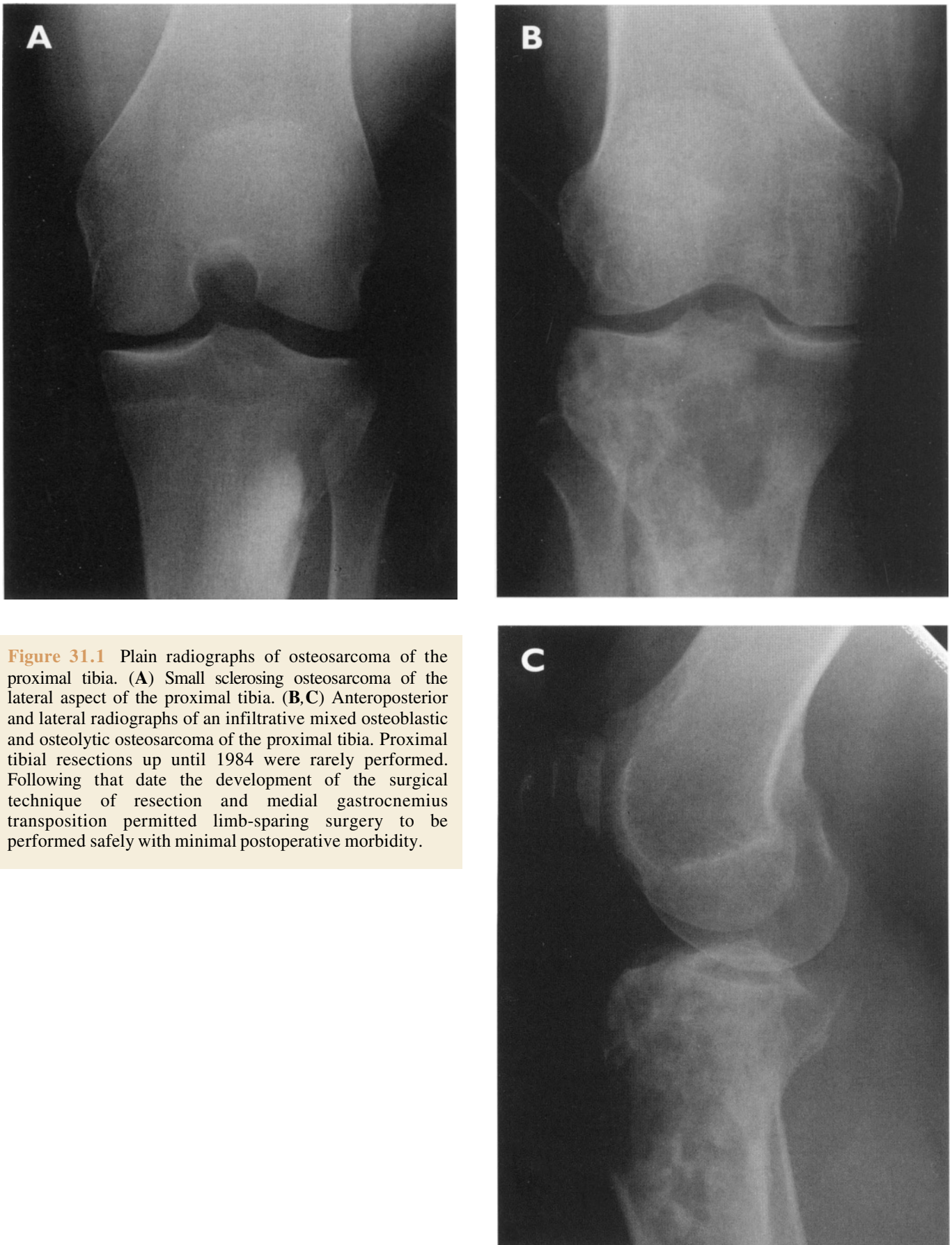


Figure 31.1 Plain radiographs of osteosarcoma of the proximal tibia. (A) Small sclerosing osteosarcoma of the lateral aspect of the proximal tibia. (B,C) Anteroposterior and lateral radiographs of an infiltrative mixed osteoblastic and osteolytic osteosarcoma of the proximal tibia. Proximal tibial resections up until 1984 were rarely performed. Following that date the development of the surgical technique of resection and medial gastrocnemius transposition permitted limb-sparing surgery to be performed safely with minimal postoperative morbidity.

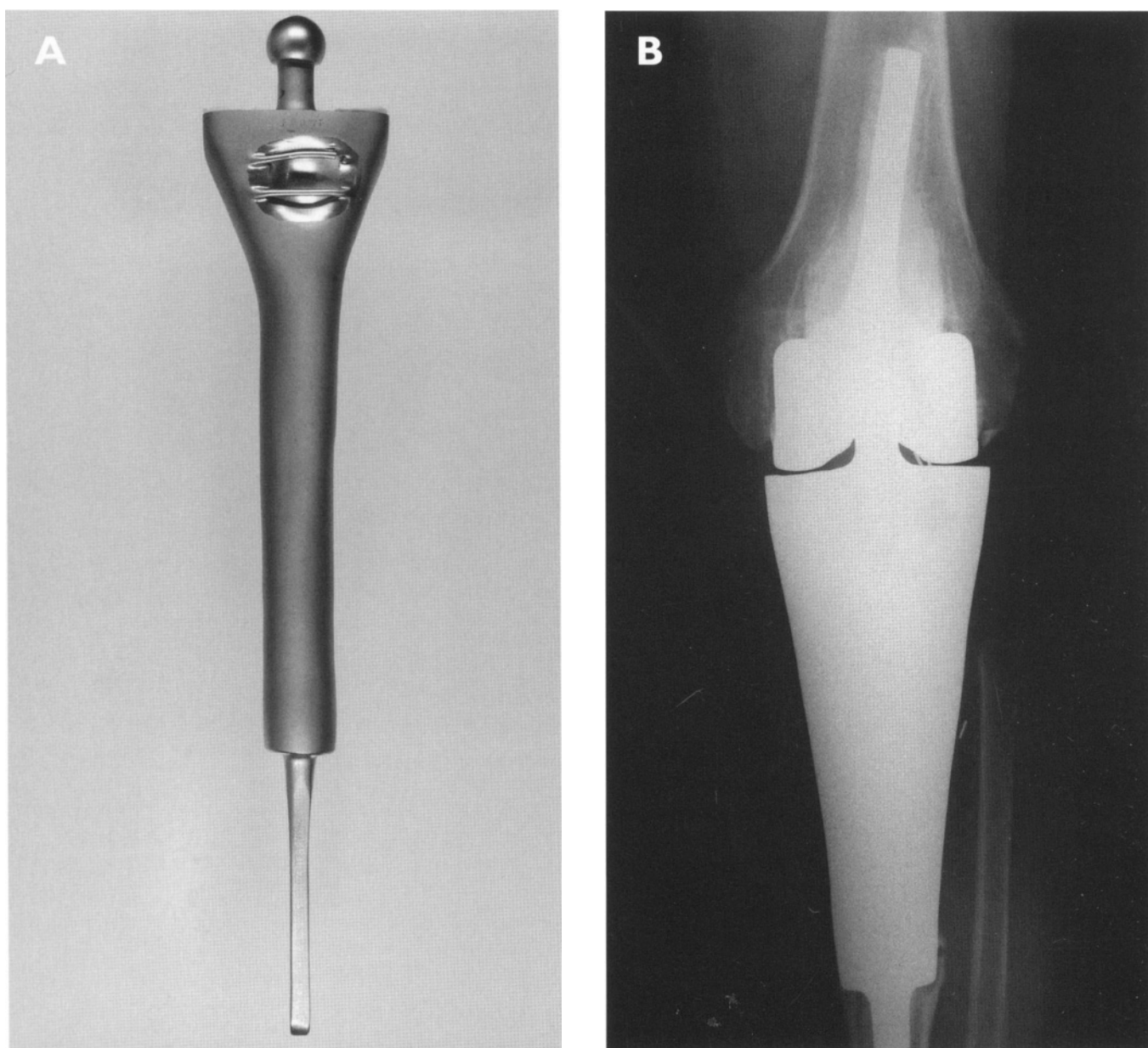


Figure 31.2 (see above and following pages) Different proximal tibial prostheses utilized over a 25-year period. **(A)** Photograph of the original custom proximal tibial replacement with a spherocentric knee component. **(B,C)** Anteroposterior and lateral radiographs of a similar prosthesis implanted. **(D)** Composite photograph of a custom and a present-day modular segmental proximal tibial replacement. Proximal tibial replacements with a modular design (Howmedica) began in 1988. **(E)** A proximal tibial component with porous coating along the entire body to permit soft-tissue attachments of the adjacent muscles as well as attachments of the patellar extensor mechanism. **(F)** Plain lateral radiograph of a similar prosthesis as in **(D)**. Note that no body was utilized between the stem and the tibial component. In general, resections of the proximal tibia are best performed when less than one-third of the length must be resected.

studies show that tumors involving the proximal tibia have a high incidence of extension and involvement of the pericapsular tissues of the tibiofibular joint. To obtain a satisfactory surgical margin while performing

a resection of the proximal tumor, it is necessary to remove this joint en-bloc, i.e. perform an extra-articular resection of the tibiofibular joint. This is routine procedure for all high-grade sarcomas of the proximal tibia.

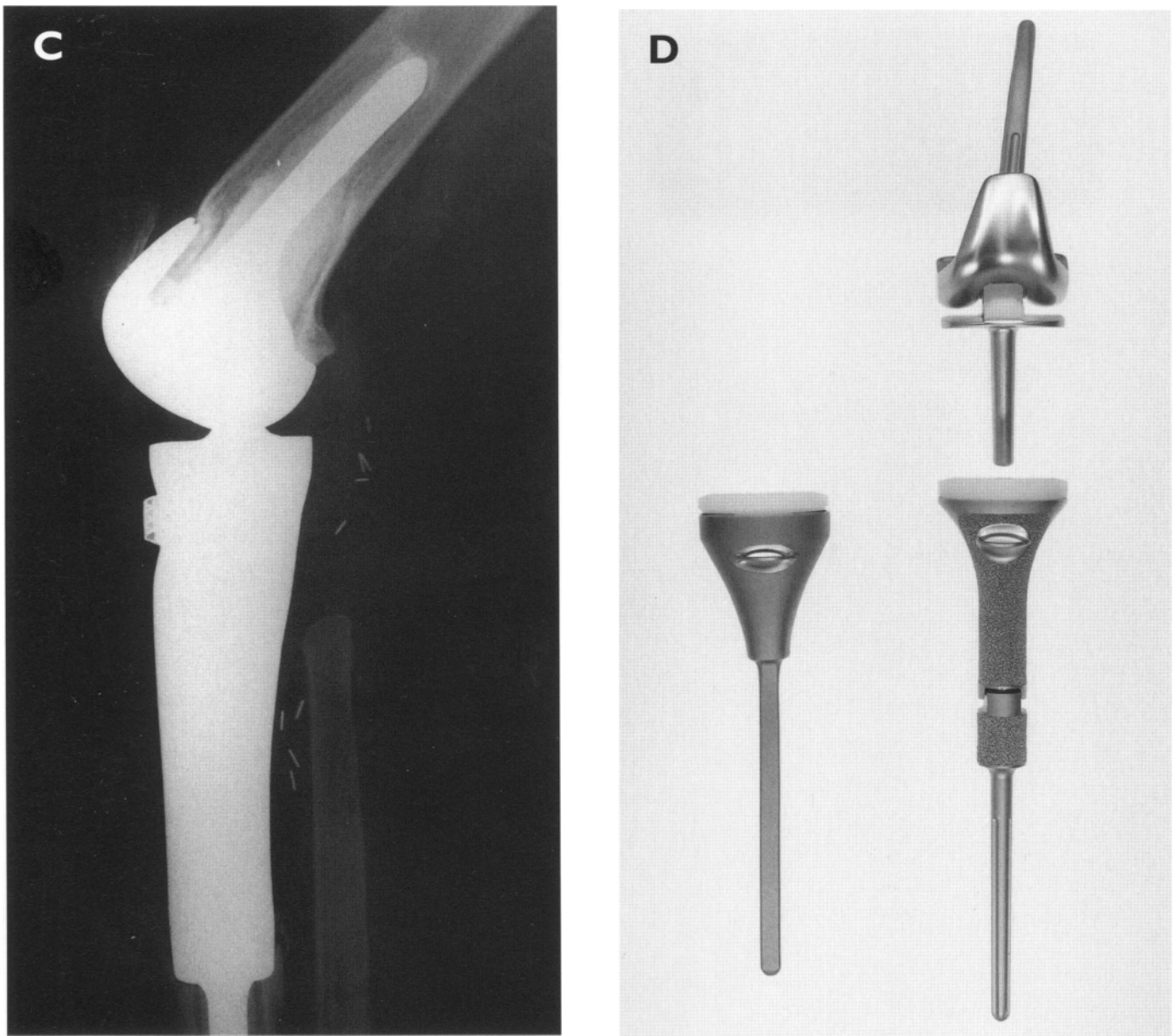


Figure 31.2 C,D

Knee Joint and Cruciate Ligaments

The knee joint is rarely directly involved by tumors of the proximal tibia unless there has been a pathologic fracture or a biopsy has contaminated the knee joint. A hemarthrosis is suggestive of intra-articular disease. MRI is the most reliable means of determining cruciate ligament involvement. If nodules are seen on the cruciate ligaments a partial extra-articular resection may be performed. Amputation is not required. Involvement of the cruciate ligaments is often not determined until the time of surgery.

Extensor Mechanism

The patellar tendon and capsular mechanism insert onto the proximal tibia and patellar tubercle. Reconstruction of this mechanism is essential for a functioning extremity. Traditionally, such reconstruction has been extremely difficult; as a result the surgical choices were to perform an arthrodesis or an amputation. Over the past 20 years several techniques of extensor mechanism reconstruction have been developed. The technique described by Malawer utilizes the medial gastrocnemius muscle, which provides for a soft-to-soft tissue

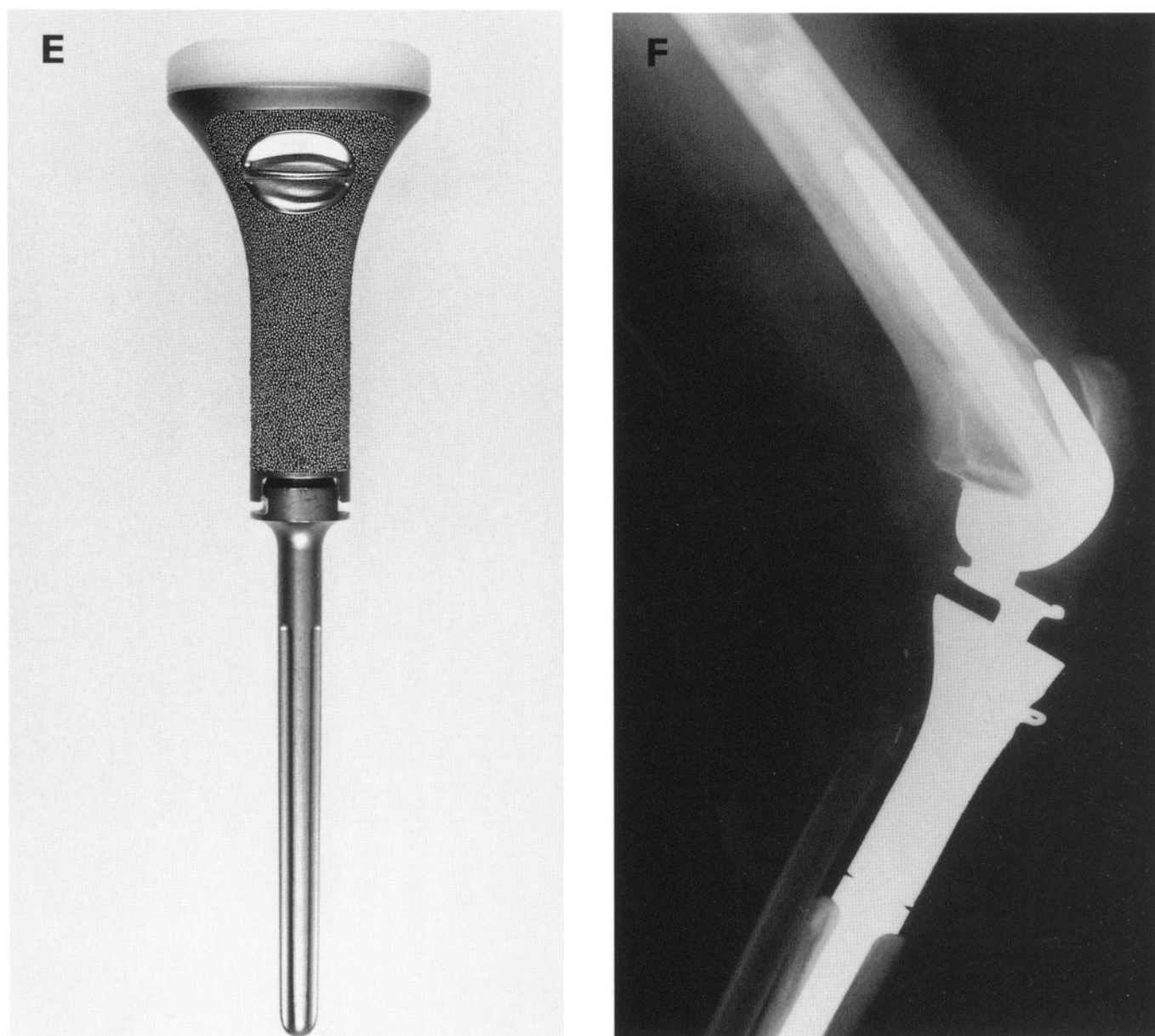


Figure 31.2 E,F

reconstruction of the extensor mechanism and has proven to be quite reliable.

Subcutaneous Location of the Tibia

The entire medial aspect of the tibia lies in a subcutaneous location. Resection and reconstruction by any technique leave the reconstructed area in a subcutaneous position. This has been a major source of primary and secondary infections, which, in turn, have necessitated an above-knee amputation. Today the routine transfer of the medial gastrocnemius muscle anteriorly, to cover the prosthesis, is a reliable method of

prosthetic coverage. This transfer also provides a method of extensor mechanism reconstruction. It is a simple and reliable means of decreasing the incidence of infection, flap necrosis, and secondary amputation.

STAGING STUDIES

Detailed radiographic analysis is necessary before surgery.

Bone Scintigraphy

Bone scintigraphy is done to rule out skip lesions and to determine the extent of local intraosseous tumor. The

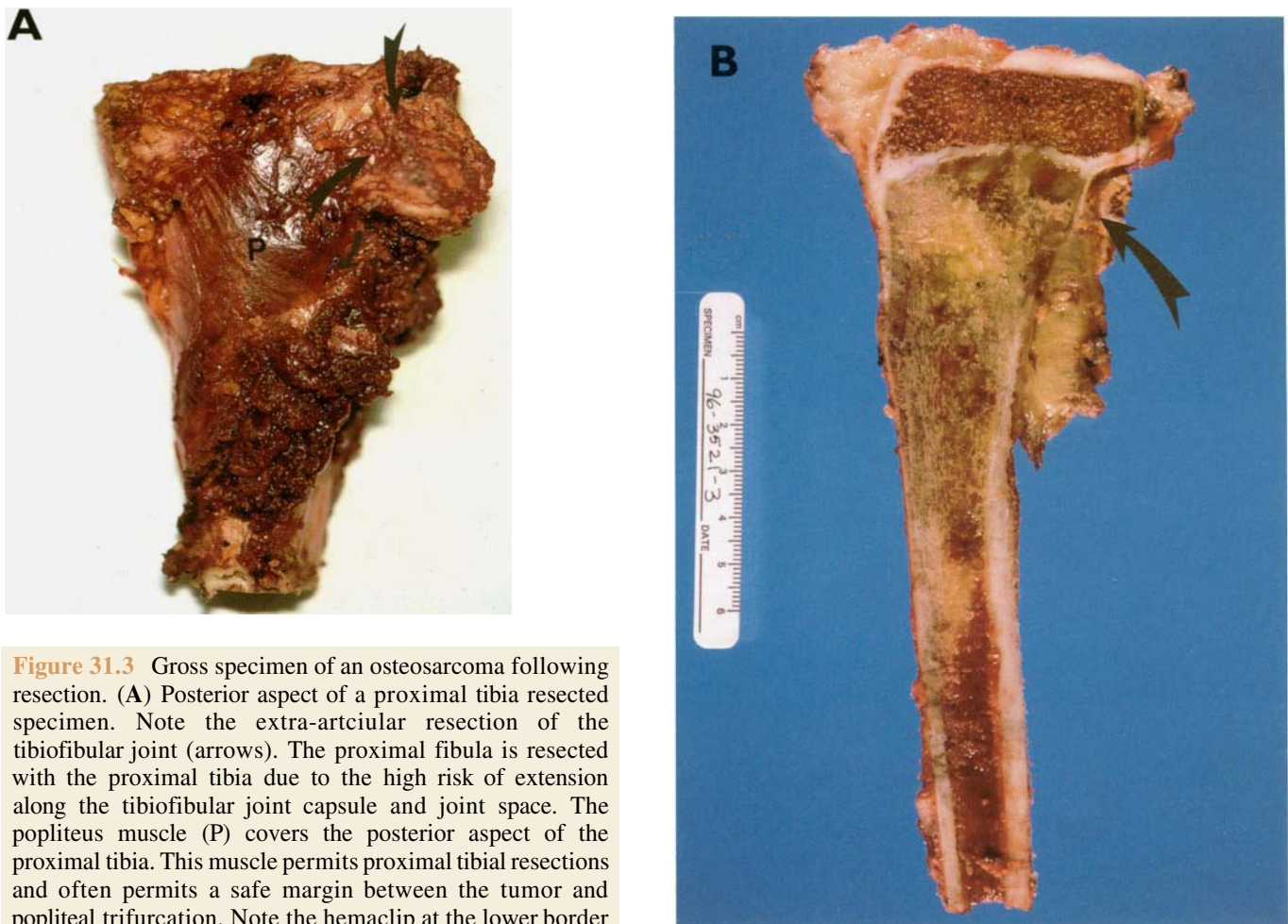


Figure 31.3 Gross specimen of an osteosarcoma following resection. **(A)** Posterior aspect of a proximal tibia resected specimen. Note the extra-articular resection of the tibiofibular joint (arrows). The proximal fibula is resected with the proximal tibia due to the high risk of extension along the tibiofibular joint capsule and joint space. The popliteus muscle (P) covers the posterior aspect of the proximal tibia. This muscle permits proximal tibial resections and often permits a safe margin between the tumor and popliteal trifurcation. Note the hemclip at the lower border of the popliteus muscle (curved arrow). This indicates the level of the anterior tibial artery that traverses from the posterior to the anterior compartment. This artery is routinely ligated to permit mobilization of the popliteal trifurcation during the initial steps of resection (see text). **(B)** A sagittal section through an osteosarcoma involving the proximal one-half of the tibia. Note, there is some tumor permeation of the epiphyseal cartilage. The tibiofibular joint was resected extra-articularly (arrow).

Figure 31.4 (see following page) Intraoperative photograph of the surgical technique of reconstruction with a modular segmental prosthesis following a proximal tibia resection and prosthetic replacement. A gastrocnemius transposition flap is the key to soft-tissue coverage and reconstruction of the extensor mechanism. **(A)** Intraoperative photograph of exposure and exploration of the proximal tibia and popliteal vessels prior to resection. The vessel loop is on the anterior tibial artery, which is routinely ligated. **(B)** Intraoperative photograph demonstrating the segmental defect following resection of the proximal tibia. The vessel loop is around the popliteal and the tibial peroneal vessels. **(C)** A Modular Segmental Prosthesis (Howmedica, Inc.) cemented into place with the patellar tendon being advanced through the loop on the prosthesis. **(D)** The patellar tendon is sutured to the loop of the prosthesis with a 3-mm Dacron tape with a cancellous bone graft within the loop to re-create a bone-tendon junction. This is later reinforced by the medial gastrocnemius muscle transposed anteriorly. **(E)** Transposition of the medial gastrocnemius muscle to cover the prosthesis as well as to aid in the soft-tissue reconstruction of the extensor mechanism. The muscle is sutured down to the transferred patellar tendon as well as sewn circumferentially to the medial and lateral capsules of the knee joint. **(F)** Medial gastrocnemius muscle is partially transposed. Note the posterior aspect of the muscle has been denuded of its deep thick fascia that permits the muscle to expand to cover a larger area. In addition, if a skin graft is necessary, it will readily take on a muscle belly in lieu of the deep fascia. **(G)** Soft-tissue reconstruction completed. The medial gastrocnemius muscle covers the entire prosthesis as well as reinforcing the patellar mechanism (GM = medial gastrocnemius muscle; arrows = level of the knee joint).

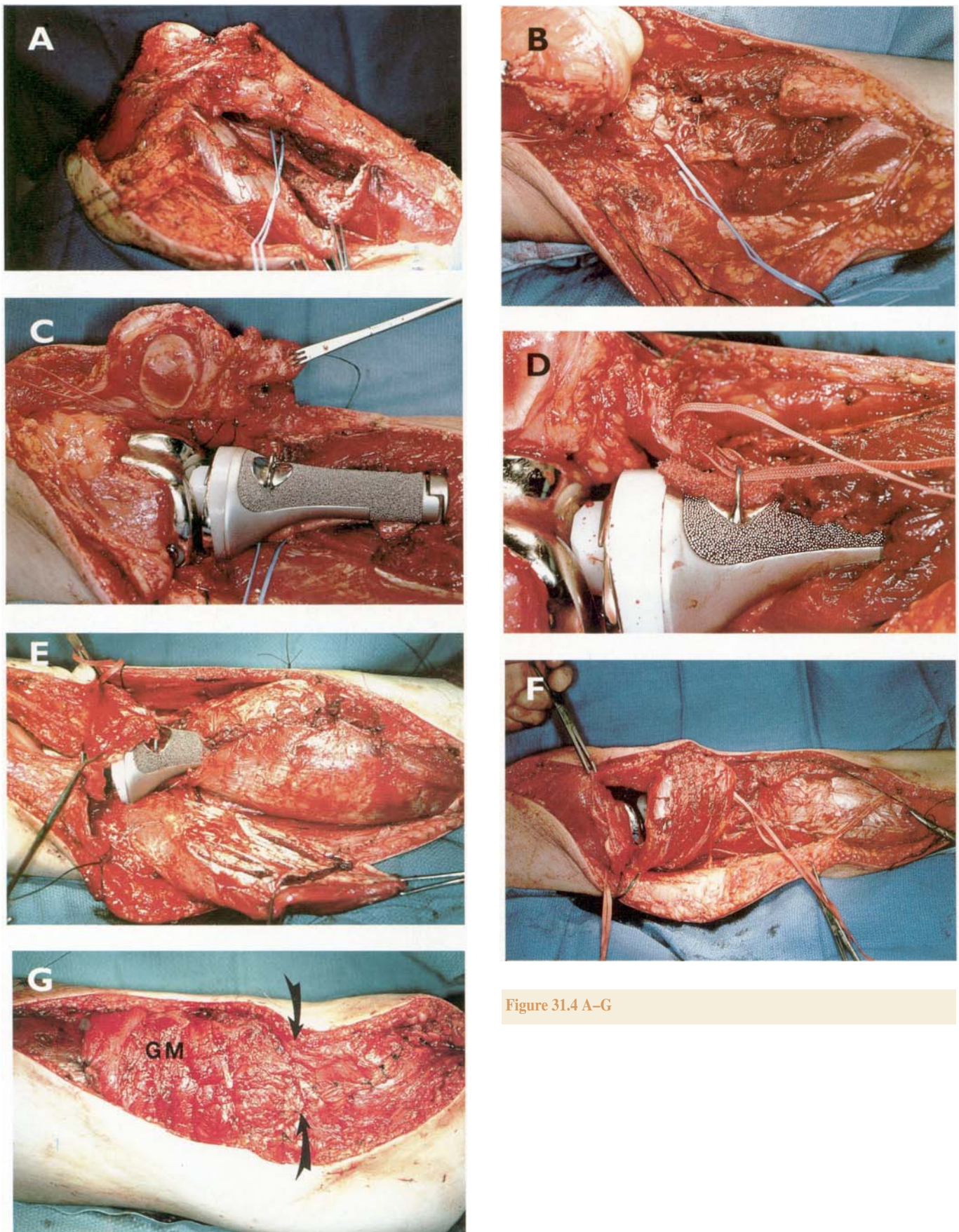


Figure 31.4 A-G

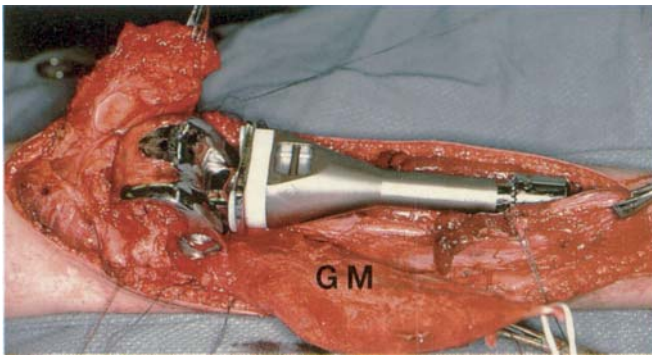


Figure 31.5 Intraoperative photograph of an expandable proximal tibial prosthesis. The patellar tendon and medial gastrocnemius muscle (GM) is utilized for soft-tissue reconstruction.



Figure 31.7 Various proximal tibial prostheses utilized during the 1980s showing a common mode of failure. The custom prosthesis on the left with porous coating shows stress fracture of the stem and similarly both expandable prostheses by different manufacturers show fracture of the stem. This was a common occurrence in the older design intramedullary stems that were often too short and narrow. In general, stems of greater than 9-mm are now utilized and rarely fracture.

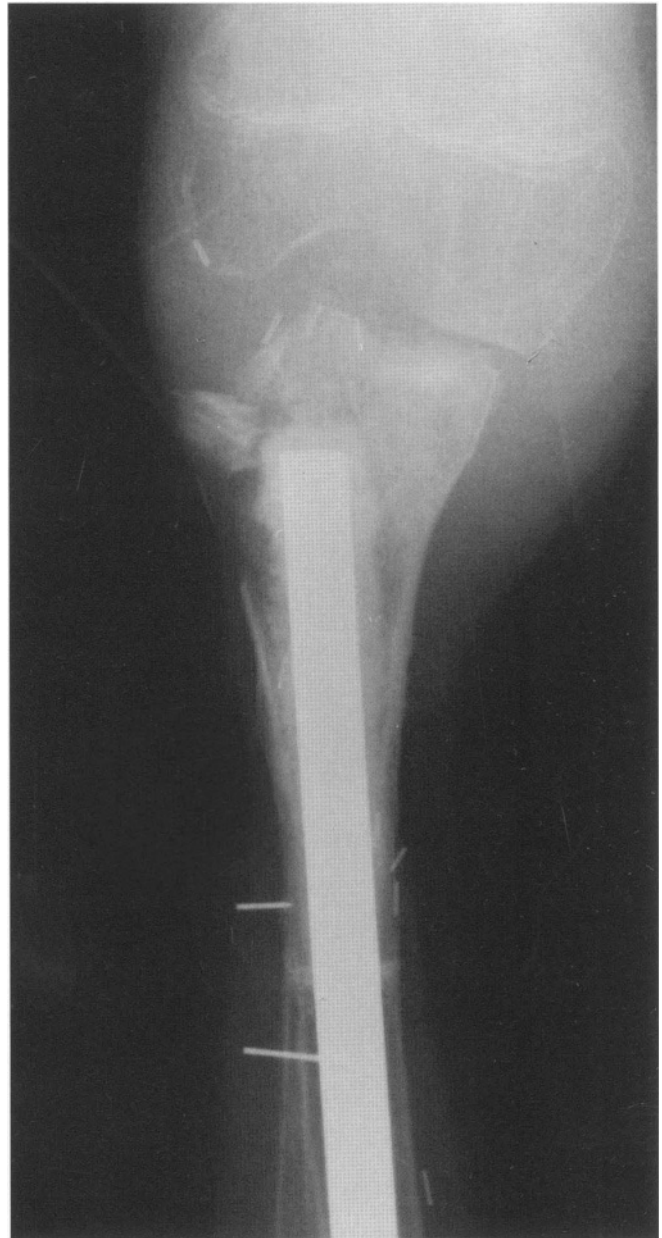


Figure 31.6 Allograft replacement. Plain radiograph 4 years following a proximal tibial allograft replacement. Note the allograft failure with collapse of the articular surface and resorption of the proximal tibial component. This patient was salvaged by a proximal tibial prosthetic replacement. In general, the authors do not recommend allograft replacements and prefer prosthetic reconstruction.

site of resection is 3–5 cm distal to the area of abnormality. At least one-third of the remaining distal tibia must appear normal.

CT and MRI

CT and MRI are useful to determine intraosseous and extraosseous extension of the primary tumor. MRI can also reveal skip lesions and soft-tissue extension. Attention is paid to the possibility of posterior extension and tibiofibular joint and intra-articular knee involvement.

Angiography

Biplane angiography (Figure 31.8) is used for local arterial evaluation, especially if CT has revealed posterior soft-tissue extension. The anteroposterior view is used to evaluate the popliteal bifurcation; of particular relevance is the presence or absence of the posterior tibial artery, which may be the sole blood supply to the leg after resection. The lateral view is required to evaluate the interval between the tibia and the neurovascular bundle. The popliteus muscle often separates a posterior tumor mass from the vessels.^{2,19} This is seen as a clear interval on the lateral angiogram and is an indication that an adequate resection margin exists. Ligation of the anterior tibial artery is almost always required. The peroneal artery may be involved by tumors with a large posterior compartment. Two of the major vessels may be ligated in a young patient, without jeopardizing the possibility of a viable and functional extremity. The posterior tibial artery is almost never involved by tumor.

BIOPSY

Extreme caution must be taken to minimize contamination of the anterior muscles, peroneal nerve, patella tendon, and knee joint when the biopsy is performed. The biopsy site must be placed along the line of the definitive incision (i.e. the anteromedial aspect of the tibia). A small core biopsy of the extraosseous tumor component is optimal. The biopsy is performed under CT or fluoroscopic guidance. There is no need to open the cortex unless the extraosseous component is not easily accessible. If the cortex must be opened, a tourniquet is used to decrease local contamination, and the cortical window is plugged with a small amount of polymethyl methacrylate (PMMA).

SURGICAL GUIDELINES (Figure 31.4)

There are three major steps involved in successful resection and reconstruction of tumors of the proximal

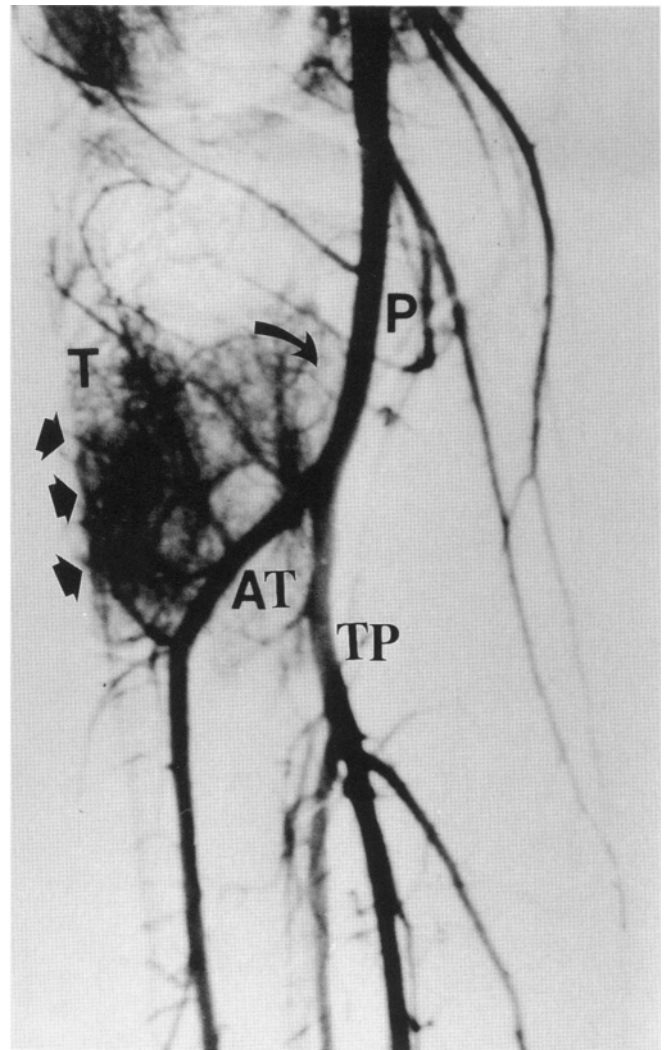


Figure 31.8 Angiogram showing lateral view of the popliteal artery. The space between tumor in the proximal tibia and the popliteal bifurcation is best appreciated by this study. The popliteal artery (P), tibioperoneal trunk (TP), and anterior tibia (AT) arteries are all visualized. It is essential that the soft tissue posterior to the tumor mass (curved arrow) be free of cancer along the popliteal artery and tibioperoneal trunk. The popliteus muscle covers the bone in this interval and usually protects the vessels from tumor invasion. A tumor (T) blush (small arrows) is seen anteriorly. (Clinical Orthopedics February 1989 Volume 239 pages 231–248)

tibia: (1) resection of the tumor, (2) reconstruction of the skeletal defect and knee joint with a modular prosthesis, and (3) reconstruction of the extensor mechanism and soft-tissue coverage of the prosthesis with the medial gastrocnemius flap.

Key issues to be considered during the various phases of surgery include the following:

1. *Incision.* A long medial incision is made from the medial peripatella to the distal one third of the leg

posteriorly and medially. Thick fasciocutaneous flaps must be developed to avoid skin necrosis.

2. *Early popliteal exploration.* The popliteal trifurcation must be explored early to determine if the tumor is operable, especially if it is in a posterior location. The popliteal space and trifurcation are exposed by detaching the medial gastrocnemius muscle and splitting the soleus muscle. A key to a successful approach to the popliteal trifurcation, especially when there is a large posterior mass displacing the vessels, is to first expose the popliteal space by identifying and detaching the origin of the medial gastrocnemius muscle and the insertion of medial hamstring muscles. The popliteal artery can be easily identified in normal tissue and be traced distally around the popliteus muscle.
3. *Tibiofibular joint resection.* This resection is performed through the same incision; a lateral flap is developed to permit exposure to the proximal fibula. The peroneal nerve must be exposed and retracted prior to resection.
4. *Exposure of the knee joint.* The capsule is transected circumferentially approximately 1 cm away from the tibia and the patellar tendon, to avoid contamination. The cruciate ligaments are visually explored. If there is any evidence of tumor nodules, the femoral condyle is later resected en-bloc with the proximal tibia, and a trans- or intra-articular resection is not performed.
5. *Soft-tissue and extensor reconstruction.* The medial gastrocnemius muscle is used for reconstruction. This provides a safe and reliable method of reconstructing the extensor mechanism as well as coverage of the prosthesis, which is essential to prevent early or late infections.
6. *Doppler examinations.* Doppler is utilized to check the pulses distally and at ankle level after the prosthesis is cemented. To prevent any spasm, the vessels are protected throughout the operative procedure with a papaverine-soaked sponge.

TECHNIQUE OF MEDIAL GASTROCNEMIUS TRANSFER AND PATELLAR MECHANISM RECONSTRUCTION

The technique for reconstruction of the patellar mechanism and coverage of the proximal tibia is based on the anterior transfer of the medial gastrocnemius muscle. Originally described by Malawer in the mid-1980s, this technique has proven to be successful and reliable.^{16,17} The medial gastrocnemius muscle is not developed until the prosthesis has been cemented into position. It is then detached distally from the midline and rotated anteriorly to cover the body of the prosthesis as well as the knee joint.

The blood supply to the medial gastrocnemius muscle is provided by the medial sural artery, which must be protected during the popliteal exploration and when ligating geniculate vessels. The medial sural artery takes off from the popliteal artery in a medial and posterior direction, whereas the geniculate vessels arise from the popliteal artery and traverse anteriorly to the distal femur and knee joint. The medial gastrocnemius muscle can be rotated both transversely and proximally to cover large defects in either direction. Approximately a 20-cm area can be covered. The medial gastrocnemius muscle is sutured to the lateral aspect of the remaining muscles of the leg circumferentially, and the capsular mechanism is sutured to the transferred muscle. The patellar tendon is sutured directly to the muscle as well as to the loops or the holes on the tibial prosthesis. Dacron tape is utilized to close the patellar tendon to the prosthesis as well as to reinforce the suture line along the gastrocnemius muscle. The reconstruction of the extensor mechanism is both dynamic (patellar tendon to gastrocnemius muscle) and static (Dacron tape fixation of the patellar tendon). This reconstruction reliably permits full knee extension and approximately 90–100° of knee flexion.

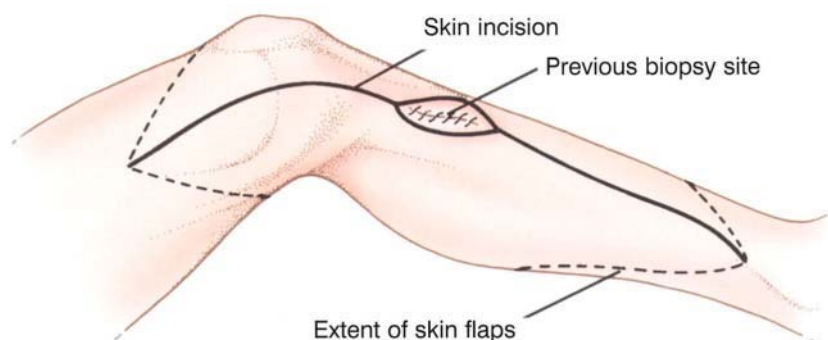


Figure 31.9 Incision. A single anteromedial incision is made, beginning proximally at the distal one-third of the femur and continuing to the distal one-third of the tibia. The approach includes excision of biopsy sites with at least a 1-cm margin. Medial and lateral flaps of skin and subcutaneous tissue are developed. Uninvolved flaps are raised with the underlying fascia to decrease flap ischemia. (Clin Orthop Rel Res 1989;239:231–248)

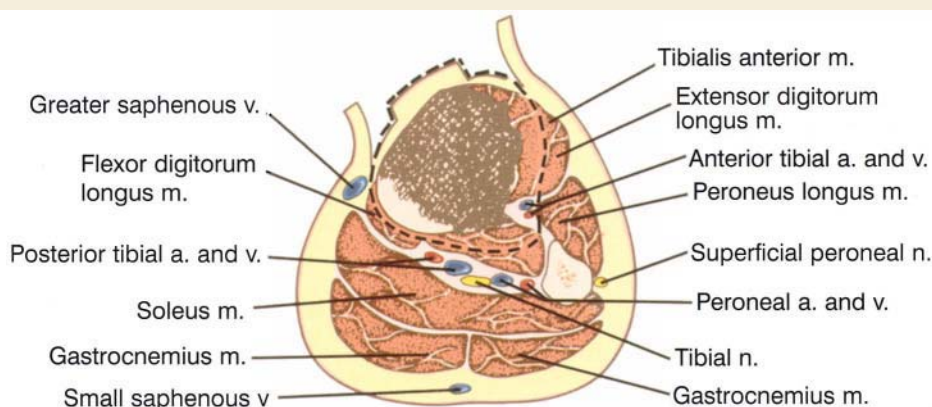


Figure 31.10 Cross-section of leg through the proximal tibia showing the planes of dissection. (Clin Orthop Rel Res 1989;239:231–248)

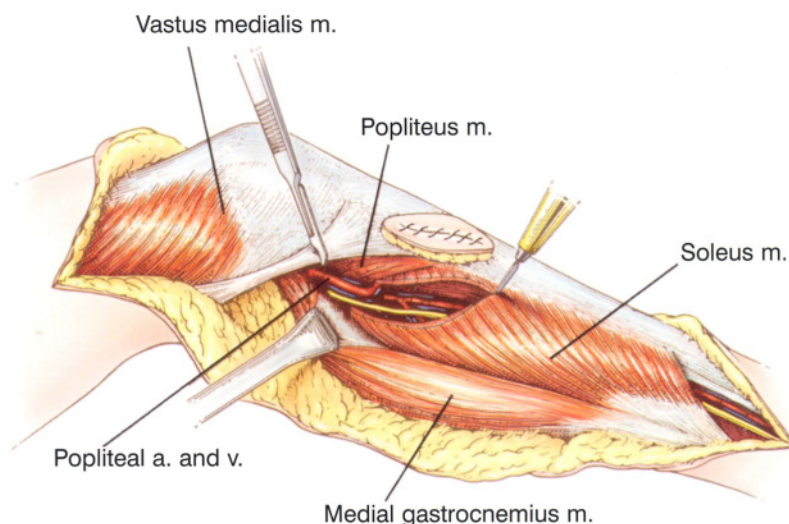


Figure 31.11 Exploration of popliteal artery trifurcation. Careful exploration of the popliteal fossa is needed to determine resectability. The medial flap is continued posteriorly, and the medial hamstrings are released at 2–3 cm proximal to their insertion to expose the popliteal fossa. The popliteal vessels are identified, and the trifurcation is initially explored through the medial approach. The medial gastrocnemius is partially mobilized, and the soleus muscle is split to expose the neurovascular structures. Care is taken to preserve the medial sural artery, which is the main pedicle to the medial gastrocnemius muscle. If the interval between the posterior aspect of the tibia and the tibioperoneal trunk (separated by popliteus muscle) is free of tumor, resection can proceed. (Clin Orthop Rel Res 1989;239:231–248)

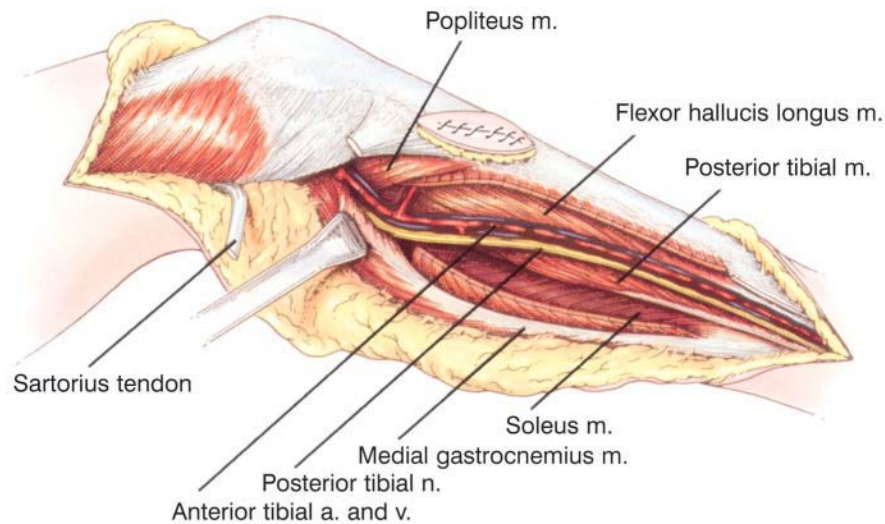


Figure 31.12 Dissection and exposure of the neurovascular bundle. Identification and mobilization of the major vessels are often difficult because the tumor has distorted the normal anatomy. Care should be taken to identify all major vascular branches prior to any ligation. The anterior tibial artery, which is the first branch of the popliteal artery, is located at the inferior border of the popliteus muscle. This artery passes directly anterior through the interosseous membrane. The anterior tibial artery ties down the neurovascular bundle to the posterior tibia and must be released. (Clin Orthop Rel Res 1989;239:231–248)

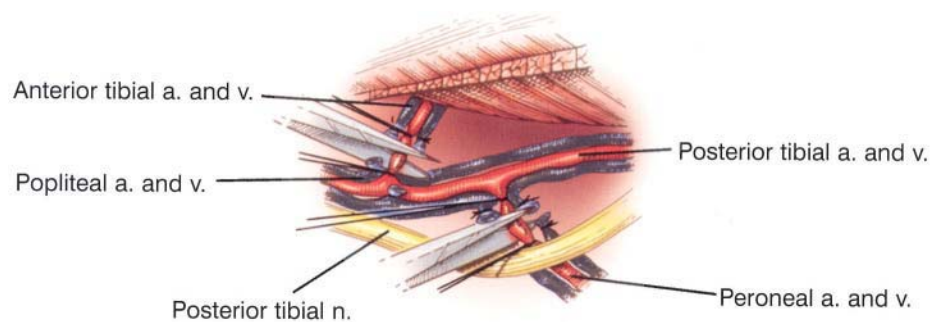


Figure 31.13 Ligation of the anterior tibial and peroneal artery and vein. Applying posterior traction proximal to the popliteal artery permits visualization of the takeoff of the anterior tibial artery and its accompanying veins. The anterior tibial vessels are individually ligated, allowing the entire neurovascular bundle to fall away from the posterior aspect of the tibia and/or tumor. If the mass is large, the peroneal artery must occasionally also be ligated. (Clin Orthop Rel Res 1989;239:231–248)

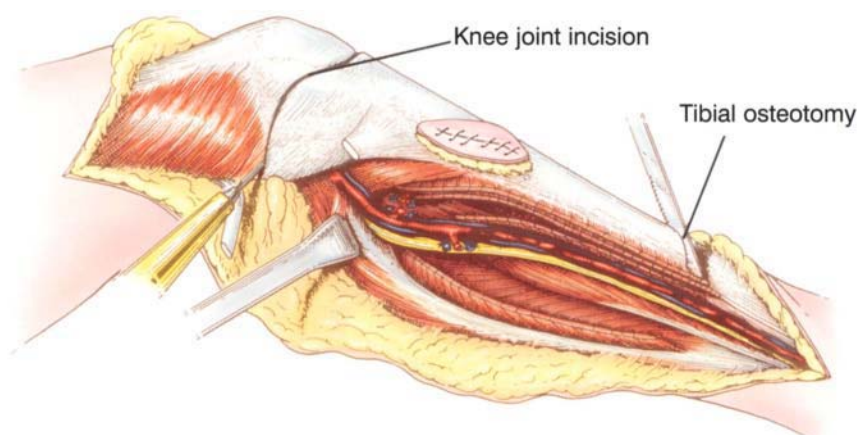


Figure 31.14 Knee joint incisions, capsular incision, and osteotomy. A small arthrotomy is performed. The meniscus and cruciate ligament are carefully evaluated. If there is no evidence of hemarthrosis (indicating tumor contamination) or direct tumor extension, an intra-articular resection is performed. The patellar tendon is sectioned 1–2 cm proximal to the tibial tubercle, and the entire capsule of the knee is detached circumferentially by electrocautery 1–2 cm from the tibial insertion. The posterior capsule is dissected carefully under direct vision after the popliteal vessels have been mobilized by ligation of the inferior geniculate vessels. The cruciate ligaments are sectioned close to the femoral attachments, and frozen sections of the proximal stumps are obtained. The capsular excision is done to the distal tibial osteotomy. (Clin Orthop Rel Res 1989;239:231–248)

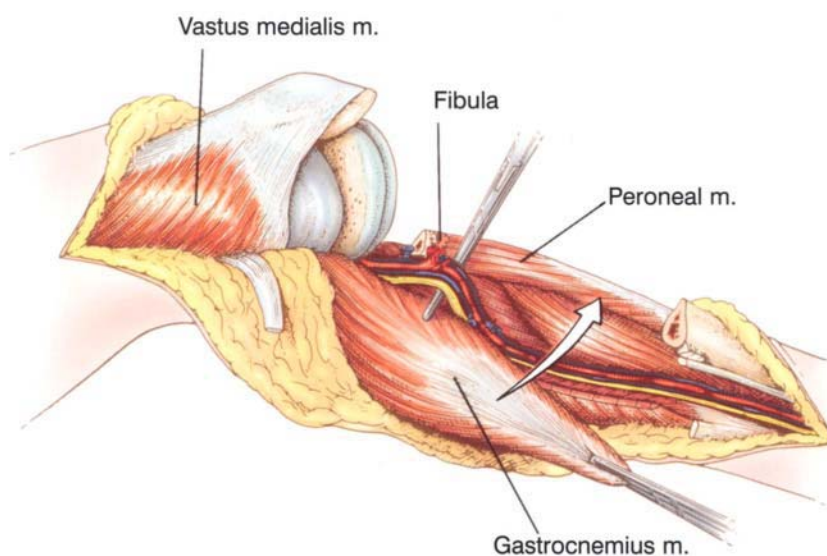


Figure 31.15 Exposure of the peroneal nerve and resection of the tibiofibular joint. A portion of the anterior tibialis muscle is routinely removed along with the tibia. The remaining anterior compartment muscles are preserved. Care must be taken to protect the branches of the peroneal nerve that innervate the anterior muscles. Posteriorly, a portion of the soleus origin and the entire popliteus muscle are left on the tibia.

The peroneal nerve is identified proximal to the fibular head and below the fascia of the biceps tendon. The biceps is transected 1 cm proximal from insertion. The peroneal nerve is freed from the proximal fibula, and the fibula is osteomized approximately 2–4 cm from its head. An extra-articular resection of the proximal tibiofibular joint is routinely performed. A sleeve of muscle is left on the joint in order to avoid inadvertent contamination by tumor. Care must be taken not to place tension on the peroneal nerve.

To release the specimen, the tibia is osteomized 5–6 cm distal to the lesion, as determined by bone scintigraphy, MRI, and CT. The intermuscular septum is released under direct vision. An intra-articular resection of the knee joint is then completed. (From Malawer and McHale.¹⁷; reprinted with permission.) (Clin Orthop Rel Res 1989;239:231–248)

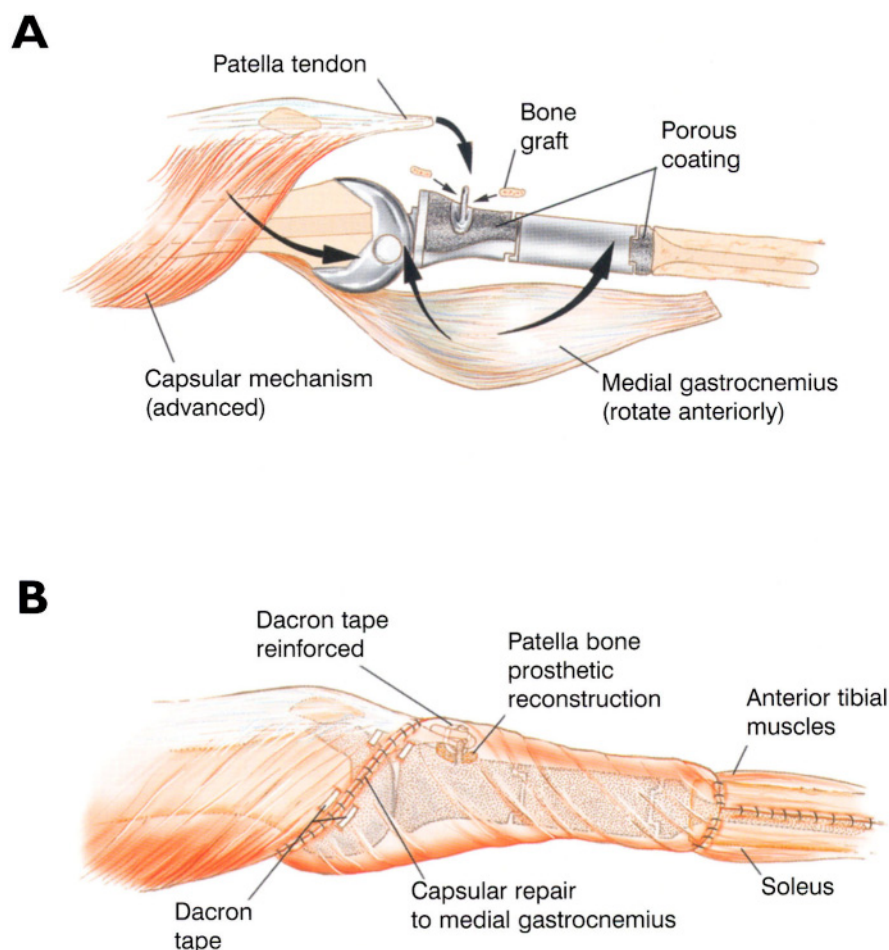


Figure 31.16 Extensor mechanism and patellar tendon reconstruction. **(A)** Schematic showing the reconstruction of the extensor mechanism. The remaining patellar tendon is sutured to the loop or the holes on the proximal tibia prosthesis with Dacron tape. Bone graft (from a portion of the resected bone from the distal femoral cuts) is placed tightly between the porous coating and the tendon. The bone graft is wedged into place. This will re-create a new "bone-tendon" junction. The medial gastrocnemius muscle is mobilized and rotated anteriorly to cover the prosthesis. The remaining medial and lateral capsular structures are advanced distally. **(B)** Completion of the extensor repair. The medial gastrocnemius muscle is now covering the prosthesis. The medial and lateral knee capsular structures are tenodesed to the superior border of the rotated medial gastrocnemius muscle. This repair is reinforced with 3 mm Dacron tape both medially and laterally. The patella tendon and bone graft are held tightly in place. The inferior border of the rotated medial gastrocnemius muscle is sutured to the soleus muscle to close over the distal end of the prosthesis. The soleus muscle may be mobilized and rotated anteriorly to close this distal corner. The soleus muscle is then sutured to the anterior leg muscles to cover the exposed tibial shaft.

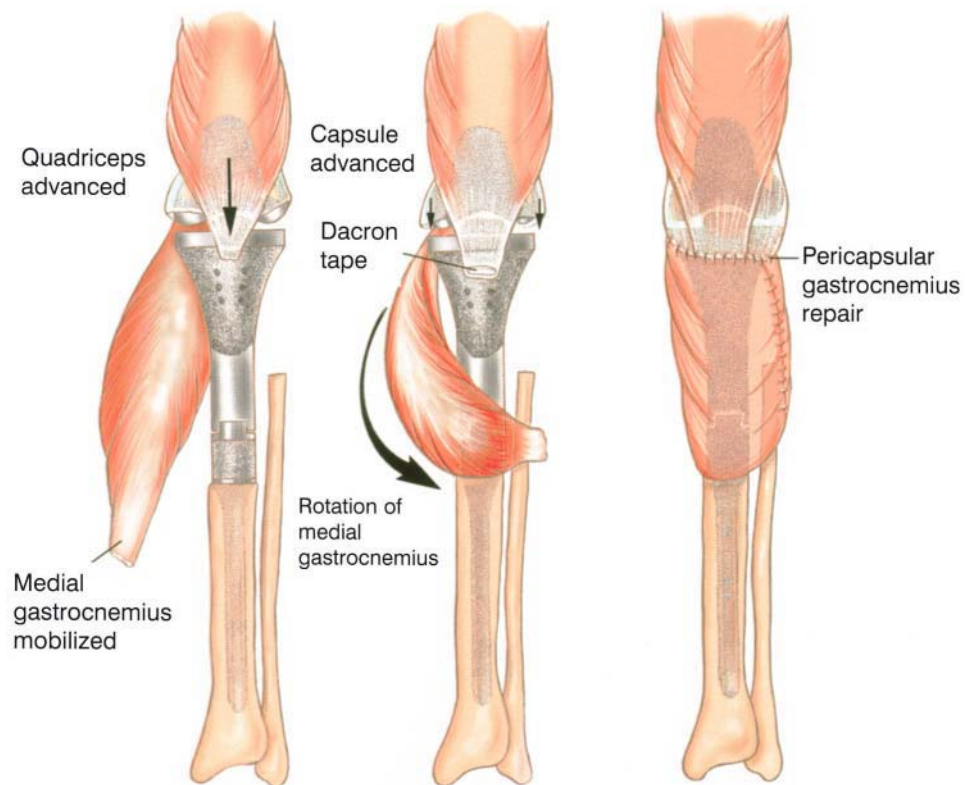


Figure 31.17 Soft-tissue reconstruction and gastrocnemius transposition. Irrespective of the type of skeletal reconstruction, a medial gastrocnemius transposition flap (GTF) is used to provide soft-tissue coverage.²¹ The medial sural artery is carefully preserved to the medial gastrocnemius muscle. The muscle graft is spread out, rotated anteriorly over the defect, and sutured to the border of the anterior muscles, forming a complete soft-tissue envelope around the prosthesis. Dacron tapes sewn into the patellar tendon are tied to a highly polished loop on the prosthetic tibia. (Clin Orthop Rel Res 1989;239:231–248)

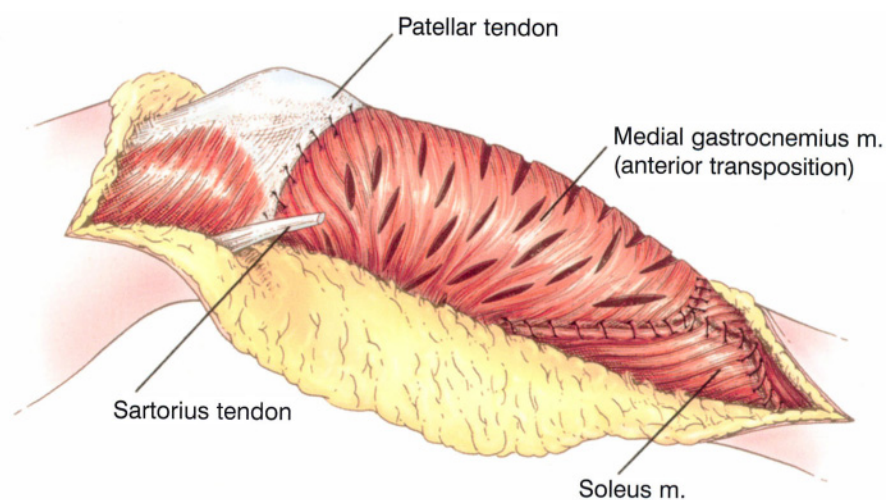


Figure 31.18 Muscular closure. The patellar tendon and anterior capsule are advanced and sutured to the transferred medial gastrocnemius muscle with nonabsorbable sutures. The proper tension on the quadriceps mechanism is determined by bending the knee through a 30–40° range of motion. The medial hamstrings are reattached to the transferred medial gastrocnemius muscle. If possible, the soft tissue posterior to the prosthesis or arthrodesis should be closed to avoid direct contact of the neurovascular bundle. At the level of the knee joint, the origins of the gastrocnemius heads are approximated; more distally, fibers of the posterior tibialis muscle and/or soleus are approximated. (Clin Orthop Rel Res 1989;239:231–248)

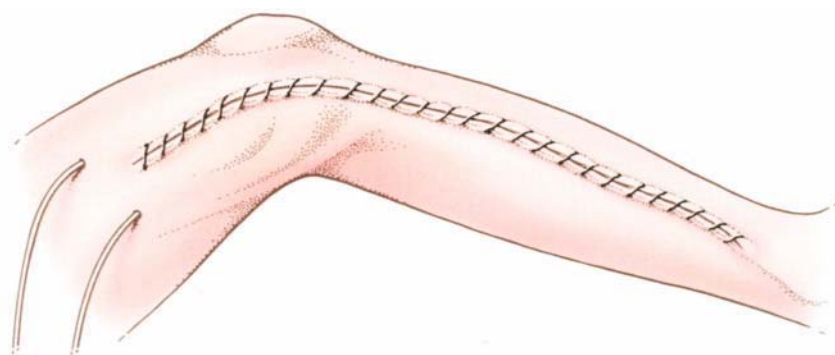


Figure 31.19 Closure of superficial fascia and skin. (Clin Orthop Rel Res 1989;239:231–248)

FUNCTIONAL AND PROSTHETIC SURVIVAL DATA

Kaplan–Meier prosthetic survival analysis, performed by Henshaw *et al.*,²⁰ was presented at the International Society of Limb-sparing Surgeons in 1998. Modular prostheses were shown to last longer than custom prostheses. The survival of the proximal tibial replacements at 10 years was approximately 78% (see Chapter 30, [Figure 30.7](#)). This is in marked contrast to reconstructions at other sites, specifically the proximal femur, distal femur, and proximal humerus, where survival of the device at 10 years approaches 95–100%. The lower survival data for prosthetic replacements at the proximal tibia are most likely attributable to the complexity of the surgical procedure and the soft-tissue reconstruction, breakage of the polyethylene component, and mechanical failure ([Figure 31.7](#)).

The incidence of infection has been dramatically decreased by the use of gastrocnemius muscle flap. The primary modes of failure are breakage of the polyethylene component within the body and aseptic loosening of the stem. Extracortical fixation is now routinely utilized for the proximal tibial replacements in the hope of creating a biological noose to prevent aseptic loosening.

POSTOPERATIVE MANAGEMENT

Large closed-suction drains are utilized to prevent hematoma. The extremity is elevated for 5–10 days to prevent edema of the flaps. If the flaps develop areas of ischemia they are allowed to demarcate and are excised at 10 days after surgery, and the underlying muscle is covered with a split-thickness skin graft. Patients with knee fusions are placed in a long-leg cast until there is radiographic evidence of bone healing (usually within 3–4 months). The patient is then fitted for a long-leg brace, which is worn for approximately a year. Patients with arthroplasty are immobilized for 3 weeks in a long-leg cast to permit healing of the extensor mechanism to the gastrocnemius transfer. A long-leg brace with the knee restricted to 0–30° is then fitted. Rehabilitation emphasizes extensor strength rather than flexion. Knee flexion is increased only after full active extension has been obtained.

Rehabilitation

The technique of rehabilitation following a proximal tibial replacement is the opposite of that following a distal femoral replacement or total knee joint replacements in general. The consideration is the ability to regain extensor function following patellar tendon reconstruction with the medial gastrocnemius muscle.

We believe that full extension must be obtained before knee flexion is attempted. Therefore, we do not utilize continuous passive motion machines following tibial replacement, and we do not permit any knee flexion, passive or active, until the patient can fully extend the limb against gravity. We anticipate approximately 90–110° of knee flexion but are not willing to jeopardize full knee extension. An extension lag is extremely detrimental to the ability to ambulate normally, especially without a limp, whereas some loss of flexion is of relatively minimal consequence.

DISCUSSION

Patients with proximal tibial osteosarcomas generally have a higher survival rate than those with femoral tumors, probably because the former tumors are smaller and generally detected earlier.^{13–15} Proximal tibial sarcomas tend to be smaller and have less of an extrasosseous component than such lesions have in other locations. Posterior extension and vascular involvement are rare; when extension does occur, the popliteus muscle often acts as a barrier to involvement of the popliteal and tibioperoneal arteries.¹⁹

Between 1978 and 1985, 11 of 21 patients presenting with sarcomas of the proximal tibia at our institution underwent limb-sparing resection utilizing a custom rotating hinge or spherocentric prosthesis ([Figure 31.4](#)).¹⁷ The remainder, most of whom were treated prior to 1980, underwent an above-knee amputation. Since 1988 the Modular Replacement System has been utilized for reconstruction. No arthrodeses were performed. The technique and surgical approach described here are reliable and have decreased the previously high complication rates. They permit a choice of reconstructive procedures (i.e. arthrodesis, prosthesis, or allograft) ([Figures 31.5–31.7](#)). Contraindications to resection generally include sepsis or local contamination, significant posterior tumor extension, or the absence of a posterior tibial artery. We believe that all patients with tibial sarcomas should be considered as potential candidates for limb-sparing procedures and should undergo appropriate staging studies to determine resectability. Accurate radiographic studies are essential. Biplane radiography and angiography, in conjunction with CT, MRI, and bone scintigraphy, accurately depict local tumor extent.

Angiography ([Figure 31.8](#)) is particularly helpful in this anatomic location, where anomalies and vascular distortion make dissection difficult. Because the tibiofibular joint is at high risk for microscopic capsular involvement, we routinely perform an extra-articular resection and do not rely upon imaging studies for that determination.

The location and technique of the biopsy are major determinants of the outcome of a limb-sparing resection, especially in this location. Appropriate technique is essential to avoid contamination of the anterolateral muscles, peroneal nerve, popliteal space, and knee joint. To minimize contamination we recommend a small core biopsy of the medial flare of the tibia that is in line with the definitive incision.

The technique of gastrocnemius reconstruction described (see Figure 31.15) here has proven to be a reliable method of soft-tissue coverage and reconstruction of the extensor/ patellar mechanism.^{21,22} Reconstructing this mechanism has heretofore been a major barrier to a successful outcome of an arthroplasty. Several techniques of extensor mechanism reconstruction have been attempted, including direct suture to the prosthesis or allograft and osteotomy of

the fibula with attachment to the lateral collateral ligament.²³ The muscle transfer technique described in this chapter uses muscle-to-muscle attachment to provide two important functions: first, it covers the prosthesis, which reduces the possibility of secondary infections; second, it provides a means for reconstruction of the extensor mechanism.

Following proximal tibial resections, intensive rehabilitation of the quadriceps is necessary. The postoperative rehabilitation following an arthroplasty of the proximal tibia is almost the opposite of that following a distal femoral arthroplasty. The aim is to avoid an extensor lag; thus, the patient is placed in a cast for 2–3 weeks to permit healing of the extensor mechanism to the transferred gastrocnemius. Immediate postoperative motion must be avoided. Active flexion exercises do not begin until extension is obtained.

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Fibular Resections

Jacob Bickels, Kristen Kellar and Martin Malawer

OVERVIEW

Primary bone sarcomas of the fibula have traditionally been treated with above-knee amputations. Increased use of limb-sparing procedures stimulated an interest in the surgical anatomy of this area and the possibility that tumors of the fibula might be safely resected. This chapter describes the surgical anatomy and resection technique for malignant lesions of the proximal, mid-, and distal fibula.

INTRODUCTION

The fibula is a rare anatomic location for both primary bone sarcomas and metastatic lesions. The proximal fibula is the most common area of the fibula to be involved by tumors; this is followed by the fibular diaphysis and the distal fibula. Osteosarcoma, Ewing's sarcoma, and giant-cell tumor are the most frequent tumor types to develop at this location.

Resection of a high-grade primary bone sarcoma of the proximal fibula necessitates an en-bloc extra-articular resection of the proximal fibula (i.e. resection of the proximal fibula with the tibiofibular joint), the anterior and lateral muscle groups, and the common peroneal nerve, which is usually involved by soft-tissue extension (Figures 32.1, 32.2). This procedure is termed a Type II resection. Because it necessitates the sacrifice of the common peroneal nerve, a Type II resection results in foot drop.¹ A Type I resection of the proximal fibula, on the other hand, involves resection of the proximal fibula with sparing of the covering muscle layer and peroneal nerve.¹ This is appropriate for benign-aggressive, low-grade malignant tumors and for metastatic lesions of the proximal fibula because

these tumors do not have a significant extraosseous component (Figures 32.1, 32.3). High-grade sarcomas of the distal fibula, which are usually characterized by involvement of tendons and nerves and lack of soft-tissue reconstruction options, are usually treated with an amputation. Fortunately, high-grade sarcomas of the distal fibula are rare.

Mechanical stability of the leg is not impaired following proximal or intercalary resections of the fibula, and reconstruction is therefore not indicated.³⁻⁵ Resections of tumors of the distal fibula, because of the lateral maleolus being a component of the ankle joint complex, do require reconstruction.^{2,6}

ANATOMIC CONSIDERATIONS AND PREOPERATIVE EVALUATION

In staging fibular tumors, emphasis is placed on the extent of bone destruction, intramedullary involvement, and soft-tissue extension. Special attention is also given to the relation of the tumor to the nerves, blood vessels, and tibia; tumor invasion of any of these structures may rule out the possibility of a limb-sparing procedure. Because of the thin cortices of the fibula and multiple muscle attachments, benign-aggressive and malignant tumors often produce early cortical breakthrough and direct muscle invasion (Figure 32.4). High-grade sarcomas are likely to invade the tibiofibular joint and posterior joint capsule and thereby necessitate an extra-articular en-bloc resection of these structures.

The patency of the anterior tibial, posterior tibial, and peroneal arteries, their anatomic relation to the tumor, and the presence of vascular anomalies are established prior to surgery using biplanar angiography; the extremity can remain functional, even if two of the three major vessels have been ligated. Type II resections of the proximal fibula cannot be performed in the presence of significant obstruction of the posterior tibial artery, because the anterior tibial and peroneal arteries will be sacrificed. In such cases a bypass procedure or an amputation should be considered.

To avoid compromising the option of limb-sparing surgery, the biopsy of a fibular lesion must be carefully planned. The biopsy tract must be the shortest way to the lesion; however, it must not violate more than one compartment and must be as remote as possible from the main neurovascular bundle of the leg. A proximal or a midfibular lesion is approached through the peroneal muscle group. To avoid contamination of the ankle joint, a distal fibular lesion is approached directly through its lateral aspect.

Above-knee amputation is considered when: (1) a malignant tumor grossly invades the tibia; (2) there is extensive multicompartamental involvement, especially

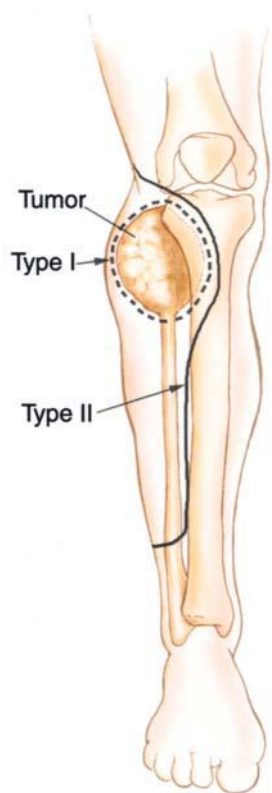


Figure 32.1 Schematic diagram showing Type I and Type II proximal fibular resections.

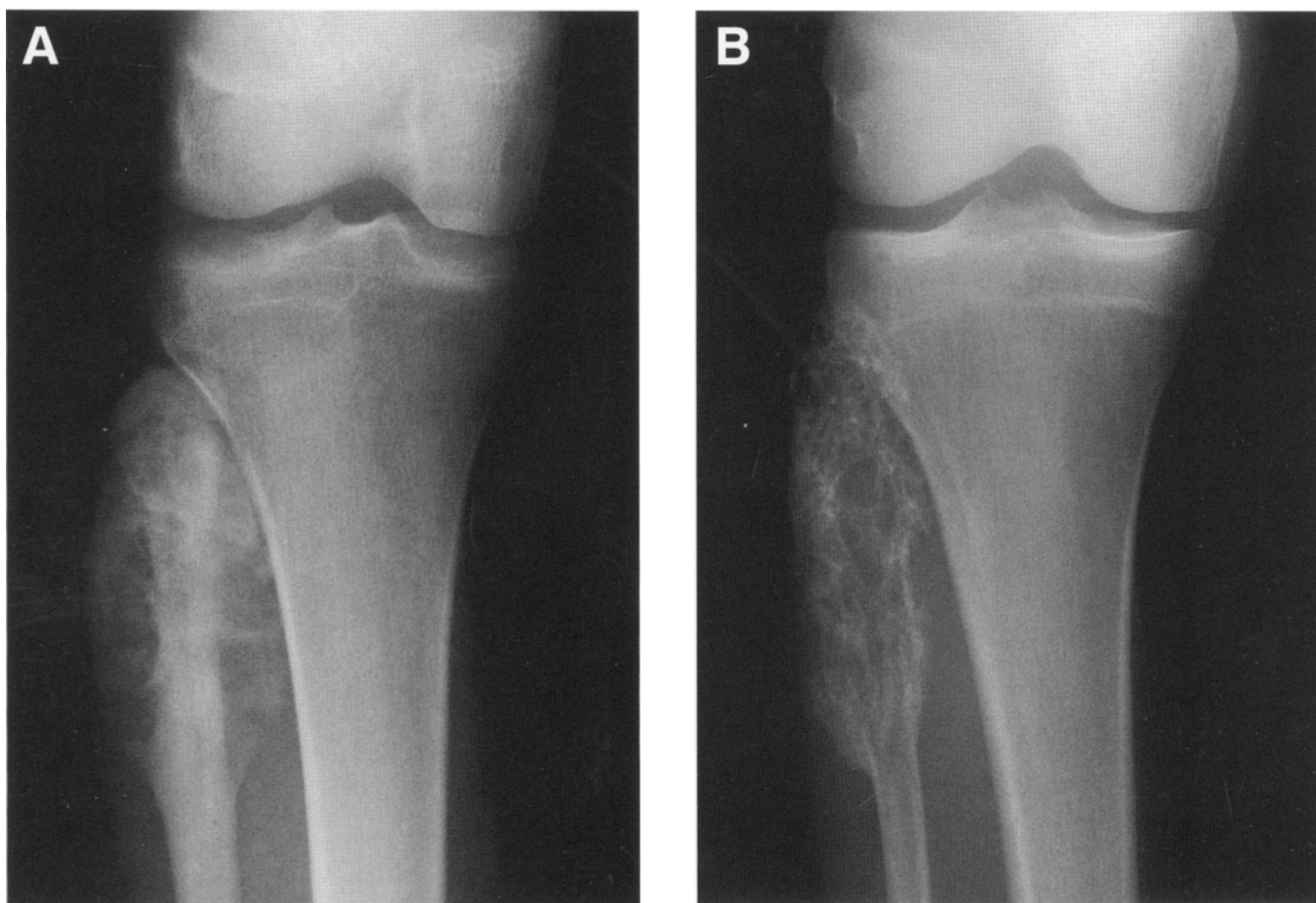


Figure 32.2 (*see also following page*) Anteroposterior plain radiographs of the proximal fibula showing (A) high-grade osteosarcomas and (B) intermediate-grade fibrosarcoma. Intermediate and high-grade primary bone sarcomas are usually associated with cortical breakthrough and soft-tissue extension. (C) A sagittal section through an osteosarcoma of the proximal fibula showing a circumferential soft-tissue extension. Wide excision of these tumors would necessitate en-bloc extra-articular resection of the proximal fibula, the surrounding muscle layer, and the common peroneal nerve (Type II resection). Extra-articular resection is not necessary for benign-aggressive or low-grade malignant tumors of the proximal fibula, which generally do not invade the joint capsule or have an extensive soft-tissue component. (D) shows a surgical specimen of a Type II fibular resection. Note the covering layer of muscles.

the posterior deep compartment; and (3) there is multi-compartmental contamination from previous biopsy or attempted resection.

SURGICAL GUIDELINES AND TECHNIQUE

A semisupine position (45° elevation of the operated side) is used to permit easy access to the anterior and lateral compartments and allow dissection of the popliteal space. The entire extremity, from the inguinal ligament to the foot, is included in the sterile field in order to allow evaluation of the distal foot pulses and execution of an above-knee amputation, if indicated.

Incision

Wide exposure of tumor, as well as of the neurovascular bundle, is mandatory. A single utilitarian approach provides a safe and wide exposure of all four compartments of the leg and popliteal fossa and allows resection of tumors of the proximal and midfibula. The incision begins posteriorly, approximately 8 cm proximal to the midpoint of the transverse popliteal skin crease, curves gently forward and distally toward the anterior tibial crest, and passes anterior to the fibular head and over Gerdy's tubercle, to a point just lateral of the tibial crest. The incision extends 5 cm distal to the level of the planned osteotomy. If a primary bone sarcoma is



Figure 32.2 C,D



resected, the previous biopsy tract with a 2–3 cm margin has to be included in the incision (Figure 32.5). A large lateral flap and a smaller medial flap are developed. Care must be taken to avoid opening of the deep fascia of any compartment at this point. Distal fibular lesions are approached via a curved incision around the lateral malleolus. Tumors of the distal fibula are not approached through a utilitarian incision; instead, the incision is placed parallel to the lateral border of the Achilles tendon, and posterior to the lateral malleolus.

Proximal Fibular Resections

A Type I proximal fibula resection is reserved for benign-aggressive and low-grade malignant tumors. It includes intra-articular resection of the proximal fibula with

2–3 cm of normal diaphysis and a thin muscle cuff in all dimensions. The anterior tibial artery is occasionally sacrificed. The peroneal nerve and its motor branches can be preserved. A Type II resection is reserved for high-grade malignant tumors. This resection includes an extra-articular resection of the proximal fibula with 6 cm of normal diaphysis, the anterior and lateral muscle compartments, the anterior tibial artery, and, occasionally, the peroneal artery, and peroneal nerve (Figure 32.6).¹

A Type II resection includes five consecutive steps: (1) exploration of the common peroneal nerve; (2) exploration of the popliteal space and artery; (3) excision of the anterior and lateral muscle compartments; (4) extra-articular resection of the tibiofibular joint; and (5) soft-tissue reconstruction (knee joint capsule, lateral gastrocnemius flap, lateral collateral ligament, and



Figure 32.3 Anteroposterior plain radiograph of the proximal fibula showing a low-grade chondrosarcoma. Although the cortices are expanded, cortical breakthrough is not evident. A Type I resection is therefore feasible.

muscle tendonesis) (Figure 32.6). Variations of this technique, as used in Type I resection, are noted.

Exposure of the Common Peroneal Nerve

The common peroneal nerve can easily be palpated near the fibular head as it passes around the inferior border of the biceps femoris muscle. If the nerve is to be preserved, as in a Type I resection, its course under the peroneus longus is identified and the peroneus longus tunnel is unroofed (Figure 32.7). After the motor branches of the peroneal nerve have been dissected, its articular branch is sacrificed to allow mobilization of the nerve posterior to the fibular head.

Exposure of the Popliteal Fossa and Identification of the Vascular Anatomy

Tumors of the proximal fibula commonly reach the midline posteriorly. Because of the distortion of the

popliteal vessels caused by the tumor, as well as the possible presence of vascular anomalies, identification of the vascular anatomy may be difficult and tedious.

The major vessels are exposed by detaching the lateral gastrocnemius muscle through its length adjacent to the fibula and, if necessary, releasing the proximal tendinous origin from the lateral femoral condyle. This exposes the underlying soleus muscle, which is similarly detached through its substance near its fibular origin. At the level of the popliteus muscle the neurovascular bundle can be easily identified. The anterior tibial artery is 2–3 cm distal to its inferior border. The peroneal artery is not seen at first because it lies in close proximity to the posterior aspect of the tibia and along the flexor hallucis longus muscle.

The posterior tibial nerve is closest to the surface and the popliteal veins are between the nerve and the posterior tibial artery that can be identified in the midline. It is crucial that the interval between the posterior fibular head and the posterior tibial and popliteal arteries be explored and evaluated early to determine whether a high-grade sarcoma is resectable. If the popliteal or posterior tibial arteries are involved, the lesion is considered unresectable unless a vascular graft is considered.

All Type II resections necessitate anterior tibial artery ligation; Type I resections, by contrast, usually allow preservation of that artery. A Type II resection may also require sacrifice of the peroneal artery. The anterior tibial artery passes directly anteriorly through the interosseous septum, tying the vascular complex down and preventing mobilization. Applying traction on the popliteal artery, a simple maneuver, permits visualization of the anterior tibial artery origin. The anterior tibial artery and the two accompanying veins may then be ligated and transected, allowing the popliteal and posterior tibial arteries to fall away from the posterior surface of the mass. Completion of the vascular dissection proceeds distally.

Excision of the Anterior and Lateral Musculature, Extra-articular Tumor Resection

The anterior and lateral musculature and the overlying deep fascia are excised. A Type I resection preserves these muscles as well as the branches from the peroneal nerve. The origin of the anterior muscles from the shaft of the tibia is transected by electrocauterization. The distal level of transection is at the musculotendinous junction. The lateral collateral ligament and the biceps tendon are released 2.5 cm proximal to their fibular insertion. The anterior tibiofibular capsule can then be identified; its posterior aspect lies under the popliteus muscle (Figure 32.8). While Type I resection preserves the tibiofibular joint, it is resected during a Type II

resection. A semicircular cut is made directly through the popliteus muscle toward the posterior aspect of the lateral condyle. Following osteotomy, it is important to inspect the lateral tibial condyle. If the knee joint capsule was exposed and opened, it should be repaired in order to prevent a potential synovial fistula. The capsule is reattached through drill holes to the posterior lateral condyle with nonabsorbable sutures. Three weeks of immobilization with the knee kept in 30° of flexion are recommended. Immobilization is not necessary following a Type I resection. Further reconstruction consists of repairing the lateral collateral ligament with nonabsorbable suture and closing and covering the exposed tibia and soft-tissue defect. This is best achieved by rotating the lateral gastrocnemius

muscle into the defect. The lateral gastrocnemius muscle can be easily rotated to cover the defect after the muscle is released close to its origin through the muscle substance and from its tendinous insertion at the distal end. Care must be taken to preserve its proximal pedicle, the lateral sural artery, throughout the dissection (Figure 32.9).

Because they entail sacrifice of the common peroneal nerve, Type II proximal fibula resections result in a foot drop. In order to avoid the need for an ankle-foot orthosis, the authors pull the peronei and extensor digitorum longus tendons, thereby advancing the foot to a neutral position, and tenodes the tendons to the tibial shaft using a 3 mm Dacron tape (Figure 32.10).

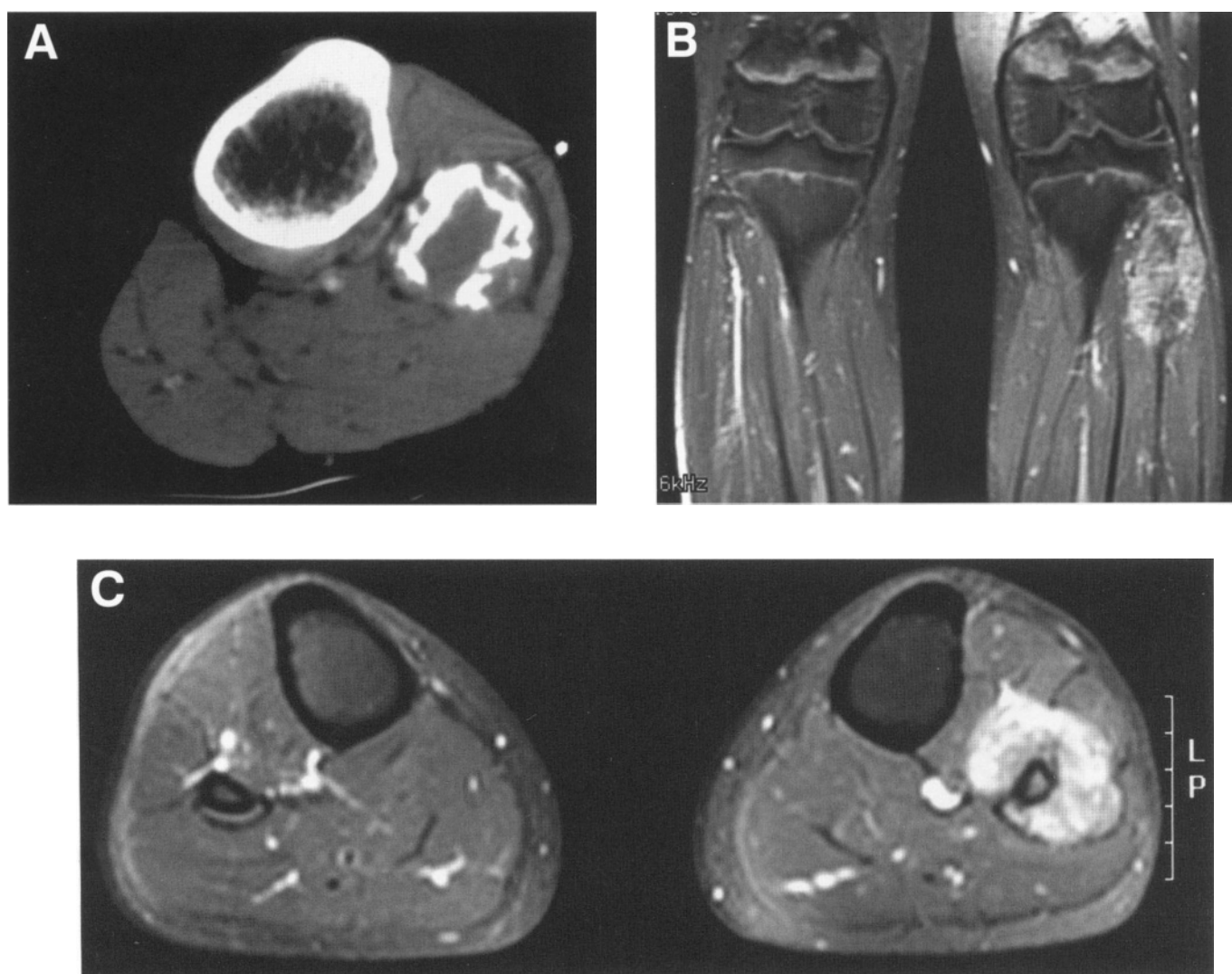


Figure 32.4 (A) Computed axial tomography of the proximal fibula showing an intermediate-grade fibrosarcoma with cortical breakthrough and extraosseous extension. (B) and (C) are coronal and axial magnetic resonance images of the proximal fibula, respectively, showing a high-grade osteosarcoma with cortical breakthrough and extension to the anterior and lateral compartments of the leg.

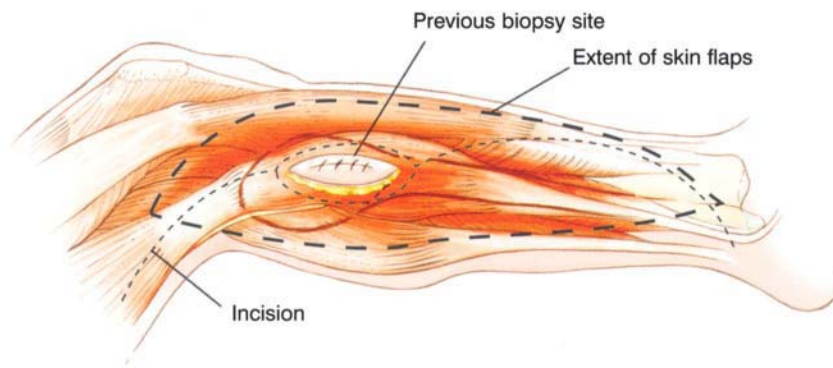


Figure 32.5 Incision and flaps. The incision extends from the biceps above the knee joint, over the mid-portion of the fibula, anteriorly to the crest of the tibia, and then curves posteriorly and distally to the ankle. This permits large anterior and posterior fasciocutaneous flaps to be developed. The anterior compartment of the leg, the lateral compartment (peroneal musculature), and the superficial posterior compartment consisting of the lateral gastrocnemius and soleus muscle are exposed. Through this incision the popliteal space and trifurcation can be explored. The biopsy site is removed en-bloc with the tumor mass. (Clin Orthop 1984;186:172–181)

MID-FIBULAR (INTERCALARY) RESECTION

Intercalary fibular resections are performed using the middle and distal portions of the utilitarian incision. The same guidelines used for proximal fibular resections apply to intercalary resections, i.e. the covering layer of muscles can be spared following resection of benign-aggressive and low-grade malignant lesions that are not accompanied by cortical breakthrough and soft-tissue extension. High-grade malignant tumors, by contrast, necessitate en-bloc resection of the muscle layer.

To expose the mid-fibula, the fascia is opened in line with the utilitarian incision. The plane between the peronei and the soleus is defined by the septum separating the two compartments. The soleus is detached from its fibular origin and, along with the lateral gastrocnemius muscle, is retracted medially and proximally to reveal the posterior crest of the fibula (Figure 32.11). The flexor hallucis longus can be spared or resected, depending on the grade and local extent of the underlying tumor. The peronei are mobilized anteriorly, and retractors are positioned underneath the fibula. Resection is then performed at the level determined prior to surgery. Care must be taken not to damage the peroneal vessels, which are posterior and parallel to the fibula.

Proximal and intercalary fibular resections do not require osseous reconstruction. Distal fibular resections, which necessitate the sacrifice of a component of the ankle joint, do require reconstruction (Figure 32.12). The authors use the ipsilateral proximal fibula to reconstruct distal fibular defects. A Type I proximal

fibula resection is performed, and the fibular head and neck are attached to the tibial plafond with a screw and to the fibular shaft with a plate (Figure 32.13).

POSTOPERATIVE MANAGEMENT

Suction drainage and prophylactic antibiotics are continued for 3–5 days. The leg is kept elevated during this time. The extremity is immobilized in 30° of flexion for 2–3 weeks to allow soft-tissue healing and posterior capsule reattachment. Full weight-bearing is allowed after the limb has been immobilized in a cast. An ankle-foot orthosis is required following a Type II resection unless tenodesis of the anterolateral compartment to the tibial shaft has been performed.

SUMMARY

Fibular resections require close familiarity with the biology of the underlying disease, the surgical anatomy of the leg, and the expected functional outcome. High-grade sarcomas of the proximal fibula necessitate resection of the covering muscle layer, tibiofibular joint, and common peroneal nerve. These structures can be saved in most patients with benign-aggressive or low-grade malignant tumors. Proximal and intercalary resections do not require osseous reconstruction; distal fibula resections are reconstructed with the ipsilateral proximal fibula. The use of a lateral gastrocnemius flap for coverage of the surgical defect and tenodesis of the anterolateral compartment to the tibial shaft as a means of stabilizing the foot in a neutral position, are recommended.

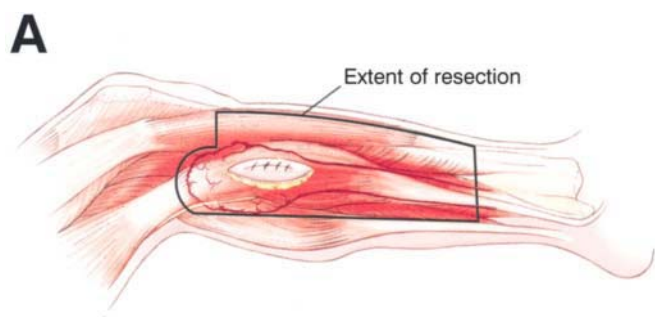
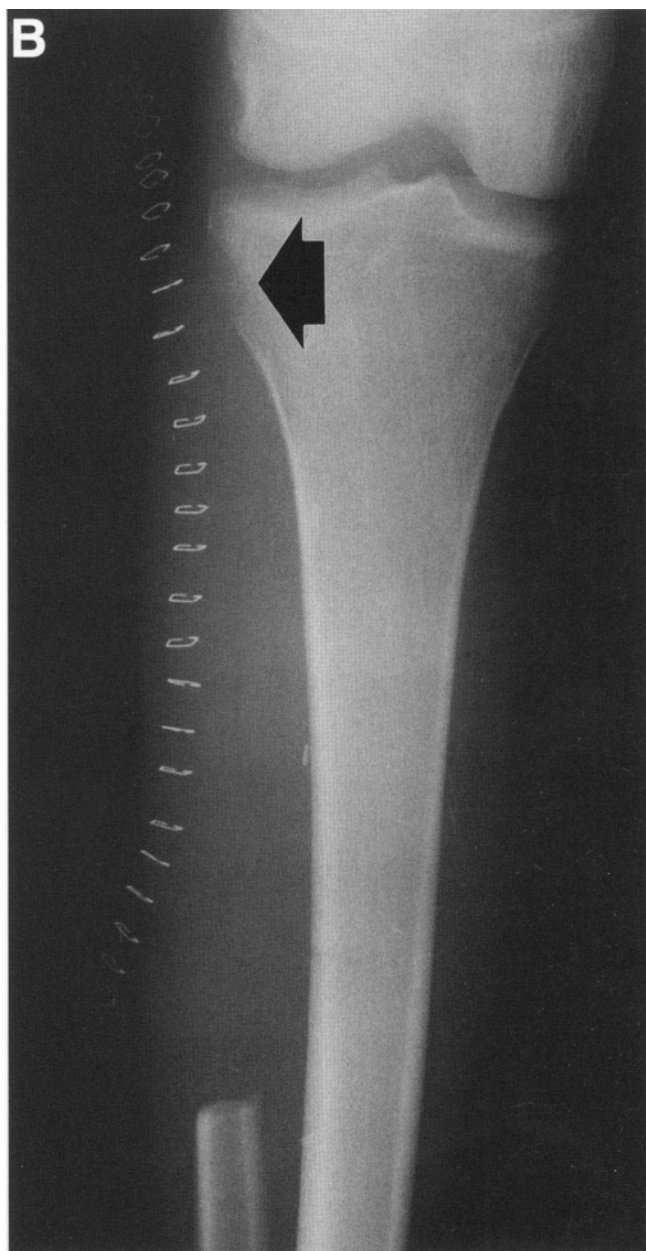


Figure 32.6A (A) Extent of resection. A Type II resection includes the proximal two-thirds of the fibula, the anterior tibial muscle compartments, and a portion of the soleus muscle which attaches to the fibula as well as the peroneal nerve. (Clin Orthop 1984;186:172–181). (B) Postoperative radiograph following a Type II fibular resection. *Note:* a portion of the adjacent lateral tibial metaphysis has been removed (arrow) indicating an extra-articular proximal tibio-fibular joint resection was performed.



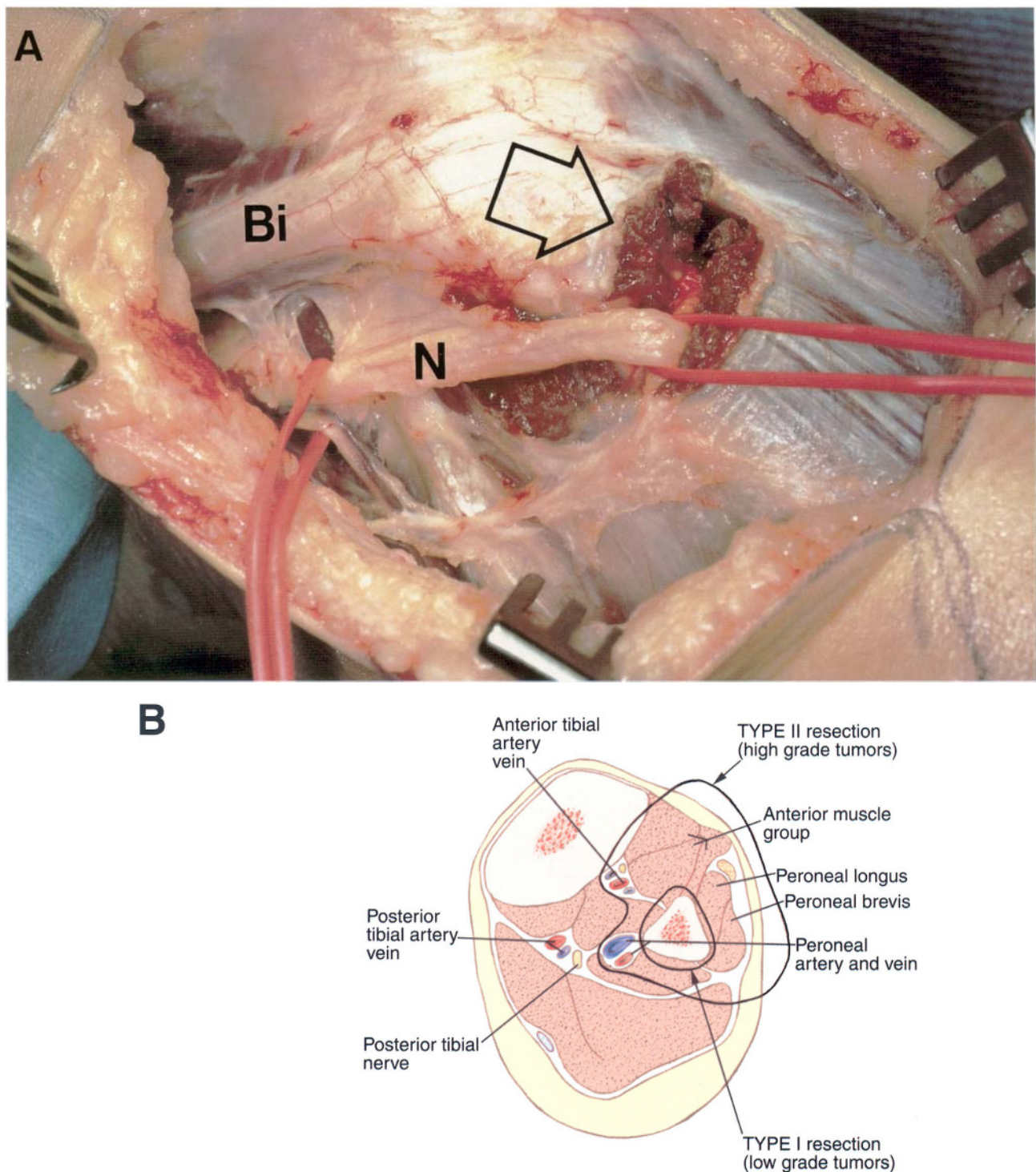


Figure 32.7 (A) Intraoperative photograph showing the peroneal nerve (N) as it enters the peroneus longus tunnel (open arrow). This tunnel has been opened to show the course of the nerve around the base of the fibular head. The biceps tendon (Bi) inserts on the fibular head away from the peroneal nerve. Vessel loops on the peroneal nerve are used to provide gentle traction for the dissection of the nerve branches as they circumnavigate the fibular neck. (B) Cross-sectional anatomy of the proximal leg showing Type I and Type II resections. A Type I resection (for low-grade tumors of the proximal fibula) includes the proximal fibula with a cuff of all adjacent soft tissues attaching to it. The major nerves and vessels, including the peroneal nerve, are preserved. Type II resection (for high-grade tumors) is a combination resection of the proximal fibula with the peroneal nerve, peroneal muscles, the entire anterior compartment musculature of the leg, and the anterior and (often) peroneal vessels. Figure 32.5A (above) is the first step in a Type I resection with preservation of the peroneal nerve.

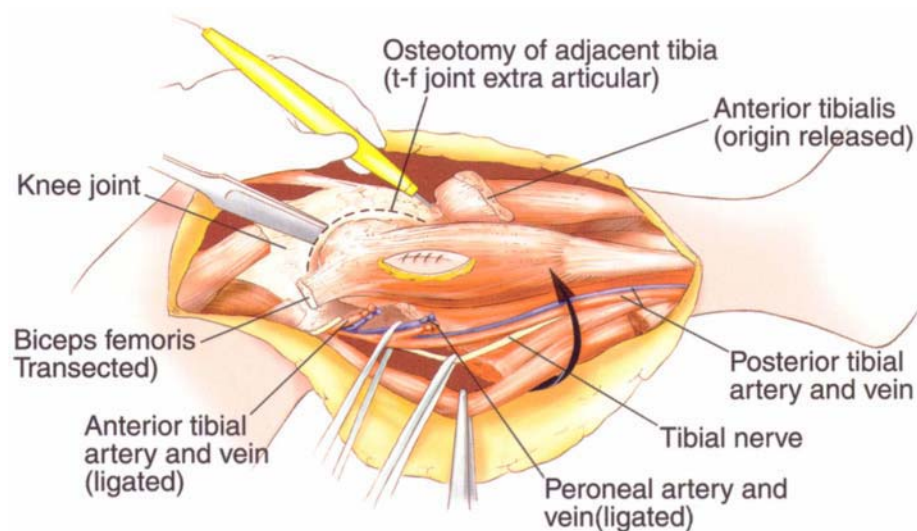


Figure 32.8 Schematic diagram of the Type II fibular resection. The resection of the proximal fibula begins with exploration of the popliteal trifurcation posteriorly. The anterior tibial artery and often the peroneal vessels are ligated if there is a large posterior component to the tumor. A resection then proceeds with release of all of the muscles attaching to the fibula posteriorly, with preservation of the tibial nerve. The peroneal nerve is ligated prior to its entry into the peroneus longus muscles. All of the tibialis muscles are released off of the tibia border and are retained on the specimen side. The final step is an extra-articular resection of the tibiofibular joint with a curved osteotome or a high-speed cutting tool, removing a portion of the lateral tibial plateau with the joint en-bloc. Care must be taken to avoid entering the knee joint. (Clin Orthop 1984;186:172–181)

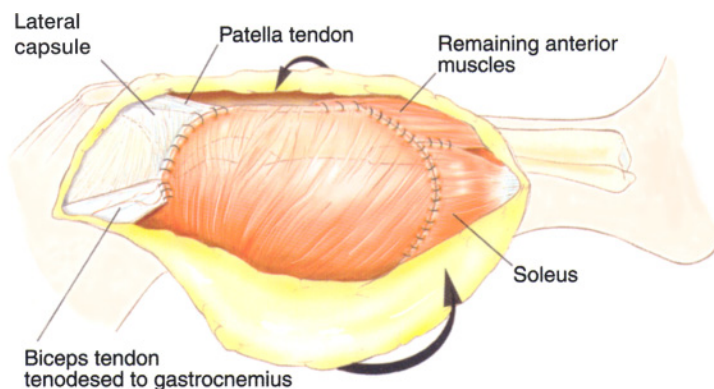


Figure 32.9 Lateral gastrocnemius muscle closure. Following resection of the fibula and adjacent muscles, the defect is closed by rotating the lateral gastrocnemius muscle anteriorly to the deep fascia covering the exposed tibia. The gastrocnemius muscle is sutured to the deep fascia as well as to the soleus muscle distally, and along the lateral capsule of the knee joint. The biceps tendon is then tenodesed to the gastrocnemius muscle. (Clin Orthop 1984;186:172–181)

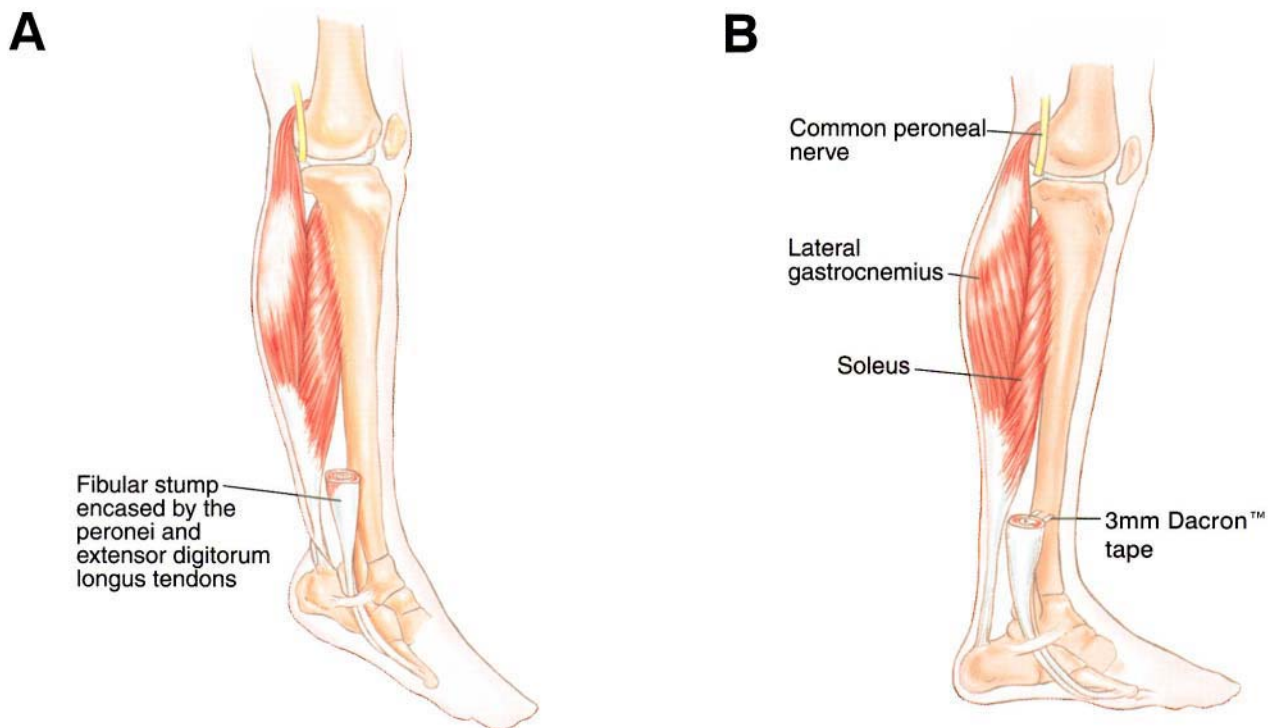


Figure 32.10 Surgical defect following a Type II resection. (A) Foot drop commonly follows Type II proximal fibula resection. (B) Tenodesis of the peronei and the extensor tendons to the tibial shaft with the foot in neutral position is routinely performed using a 3 mm Dacron tape. This procedure prevents plantar flexion and obviates the need for an ankle-foot orthosis.

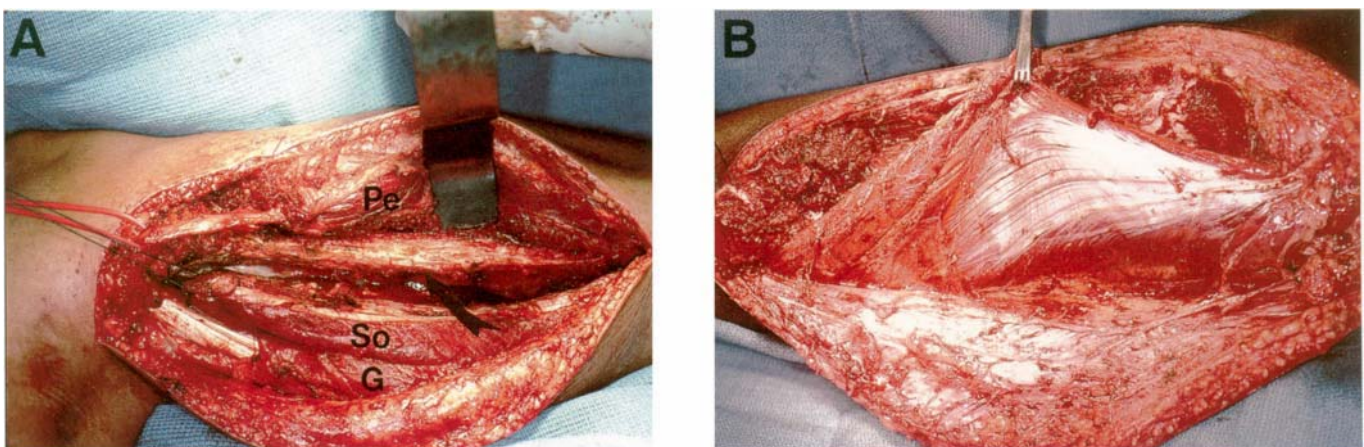


Figure 32.11 (A) Operative photograph of intercalary fibular resection. The soleus (So) is detached from its fibular origin and, along with the lateral gastrocnemius muscle (G), is retracted medially and proximally to reveal the posterior crest of the fibula (arrow). The flexor hallucis longus can be spared or resected, depending on the grade and local extent of the tumor. The peronei muscles (Pe) are mobilized anteriorly, retractors are positioned underneath the fibula, and the resection is performed at the level determined prior to surgery. (B) The lateral gastrocnemius muscle is rotated laterally to close the surgical defect.

Figure 32.12 (*right, see also following page*) A 45-year-old woman presented with a 1-year history of constant pain along the lateral aspect of her leg. (A) Anteroposterior plain radiograph of the fibula showing fibrous dysplasia of the midfibula. Intercalary fibular resection, as revealed by (B) anteroposterior and (C) lateral photographs, resulted in complete resolution of her symptoms.

A

B**C**

Figure 32.12 B,C

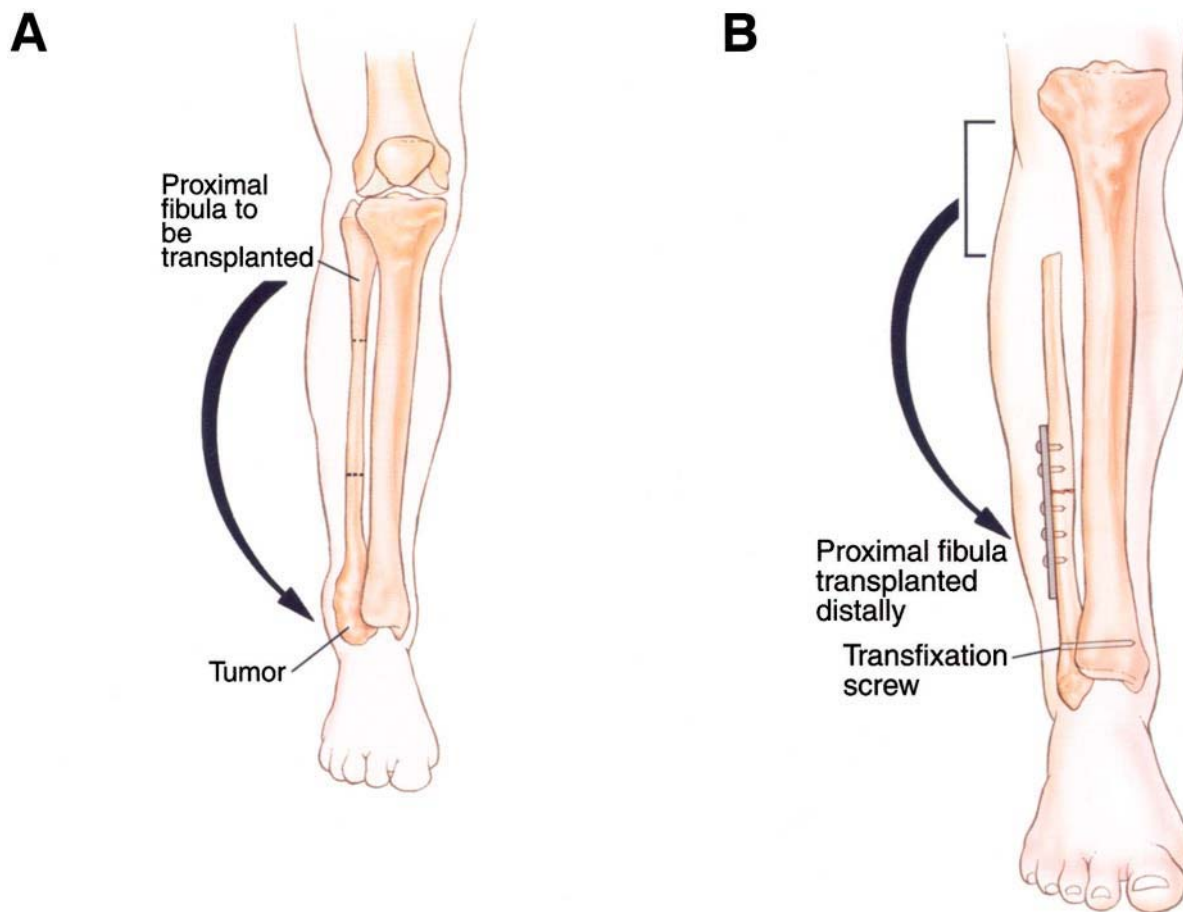


Figure 32.13 (A) A curved incision around the lateral malleolus is used for distal fibular resections. (B) The authors use the proximal fibula to reconstruct the distal fibular defect; a Type I proximal fibula resection is performed, and the fibular head and neck are attached to the tibial plafond with a screw and to the fibular shaft with a plate. This technique has permitted increased ankle stability following distal fibular resections.

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Proximal Humerus Resection. The Tikhoff–Linberg Procedure and its Modifications

Martin Malawer and James Wittig

OVERVIEW

The proximal humerus is a common site for primary osteosarcomas as well as chondrosarcomas. Metastatic tumors occasionally involve the shoulder girdle and are often treated using the same resection and reconstruction techniques. Limb-sparing resection of the proximal humerus is challenging. Despite their complexity, these resections can be performed in approximately 95% of patients with high- or low-grade sarcomas. Amputations are rarely required.

Endoprosthetic reconstruction is the most common technique for reconstructing large proximal humeral defects. It is used following both intra-articular (Type I) and extra-articular (Type V) resections (see Chapter 9). This is combined with local muscle transfers to create shoulder stability, cover the prosthesis, and provide a functional elbow, wrist, and hand.

The surgical and anatomic considerations of limb-sparing procedures of the proximal humerus and the specific surgical techniques of intra- (Type I) and extra-articular (Type V) resection and reconstruction are described in this chapter. Total humeral replacement is briefly described.

INTRODUCTION

The proximal humerus is one of the most common sites for high-grade malignant bone tumors in the adult. It is the third most common site for osteosarcoma.¹ Tumors in this location tend to have a significant extraosseous component. The proximal humerus may also be involved by metastatic cancer (especially renal-cell carcinoma) and secondarily by soft-tissue sarcomas that require a resection similar to that used for primary bone sarcomas with extraosseous extension.

Approximately 95% of patients with tumors of the shoulder girdle can be treated with limb-sparing resections. The Tikhoff–Linberg resection and its modifications are limb-sparing surgical options for bone and soft-tissue tumors in and around the proximal humerus and shoulder girdle. Portions of the scapula, clavicle, and proximal humerus are resected in conjunction with all muscles inserting onto and originating from the involved bones. Careful preoperative staging and selection of patients whose tumor does not encase the neurovascular bundle, or invade the chest wall, are required. A classification system for resection of tumors in this location is described in Chapter 9. The most common procedure for high-grade sarcomas of the proximal humerus, Type VB, is described. The authors do not recommend intra-articular resection (Type I) for high-grade tumors, due to the increased risk of local recurrence.

Optimal function is achieved with muscle transfers and skeletal reconstruction. A prosthesis is used to maintain length and stabilize the shoulder and distal humerus following resection. A stable shoulder with normal function of the elbow, wrist, and hand should be achieved following most shoulder girdle resections and reconstructions performed using the techniques described here (Figure 33.1).

INDICATIONS

Indications for limb-sparing procedures of the proximal humerus and shoulder girdle include high-grade and some low-grade bone sarcomas, as well as some soft-tissue sarcomas that secondarily invade bone (Figure 33.2). Occasionally, solitary metastatic carcinomas to the proximal humerus are best treated by a wide excision (Type I resection). The decision to proceed with limb-sparing surgery is based on the location of the tumor and a thorough understanding of its natural history. Absolute contraindications include tumor involvement of the neurovascular bundle or extensive invasion of the adjacent chest wall. Relative contraindications include chest wall extension, tumor contamination of the operative site from hematoma following a poorly performed biopsy or pathologic

fracture, a previous infection, or lymph node involvement. Recently, we have treated patients with pathologic fractures with induction chemotherapy, immobilization, and limb-sparing surgery if there is a good clinical response and fracture healing (Figure 33.3).

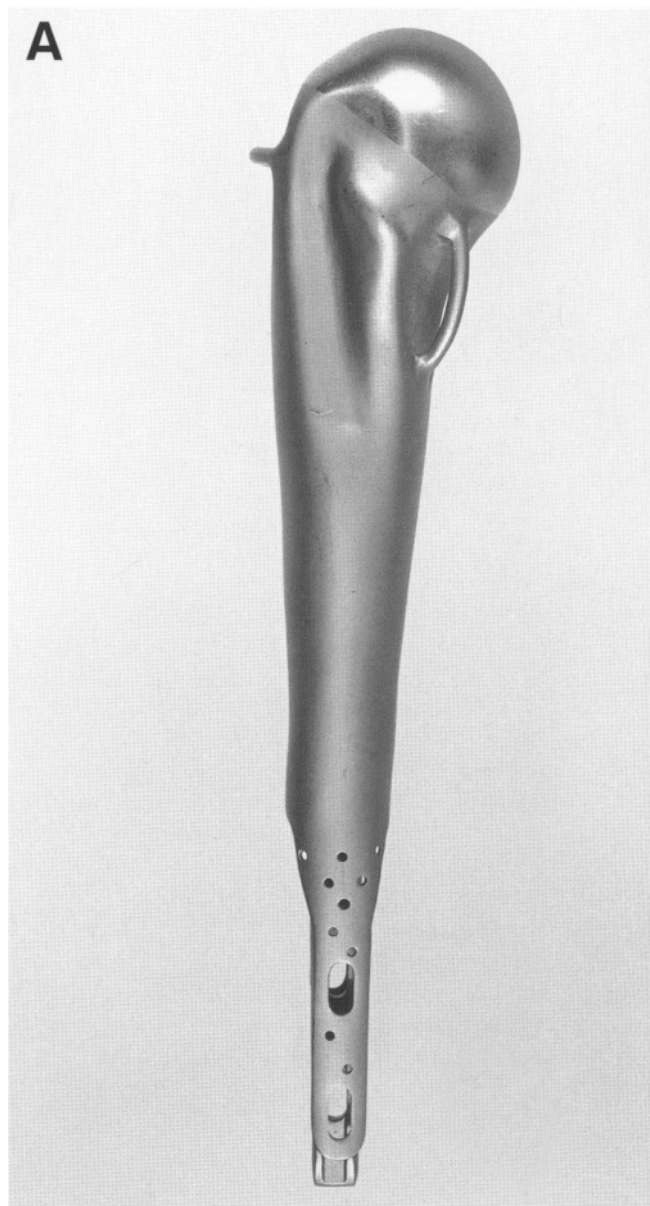


Figure 33.1 (see also following page) Proximal humeral prostheses that have been utilized within the past two decades. (A) Initial prosthesis produced by Howmedica, Inc., Rutherford, New Jersey, with external phalanges. This was a type of prosthesis that was utilized in the 1970s. (B) Custom prosthesis with porous coating along the body. This design was utilized during the mid-1980s. (C) Modular Replacement System. This prosthesis was designed in 1988 and is currently still utilized.

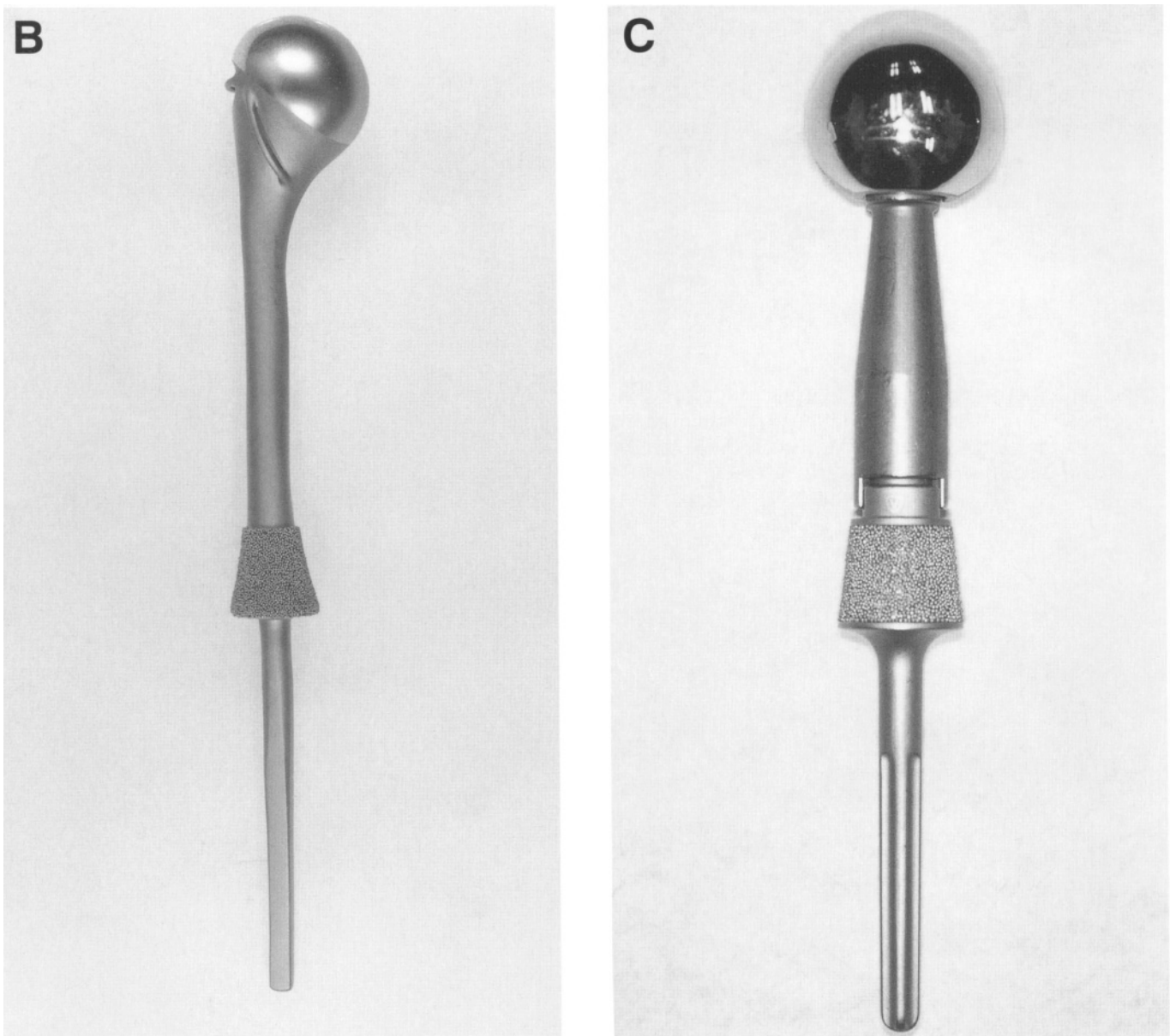


Figure 33.1 B,C

UNIQUE ANATOMIC CONSIDERATIONS

Resection and reconstruction of the proximal humerus and shoulder girdle is a technically demanding procedure. The local anatomy of the tumor often determines the extent of the operation required. One should be experienced with all aspects of shoulder girdle anatomy and the unique considerations presented; these may be summarized as follows:

Proximal Humerus

Malignant tumors often present with large soft-tissue components (Stage IIB) underneath the deltoid that extend medially and displace the subscapularis and

coracobrachialis muscles.² Pericapsular and rotator cuff involvement occur early and must be evaluated (Figure 33.4).

Glenohumeral Joint

The shoulder joint appears to be more prone to intra-articular or pericapsular involvement by high-grade bone sarcomas than are other joints. There are five basic mechanisms for tumor spread: direct capsular extension, tumor extension along the long head of the biceps tendon, fracture hematoma from a pathologic fracture, synovial spread, and direct articular spread (Figure 33.4A).

These mechanisms make patients undergoing intra-articular resections for high-grade sarcomas at greater

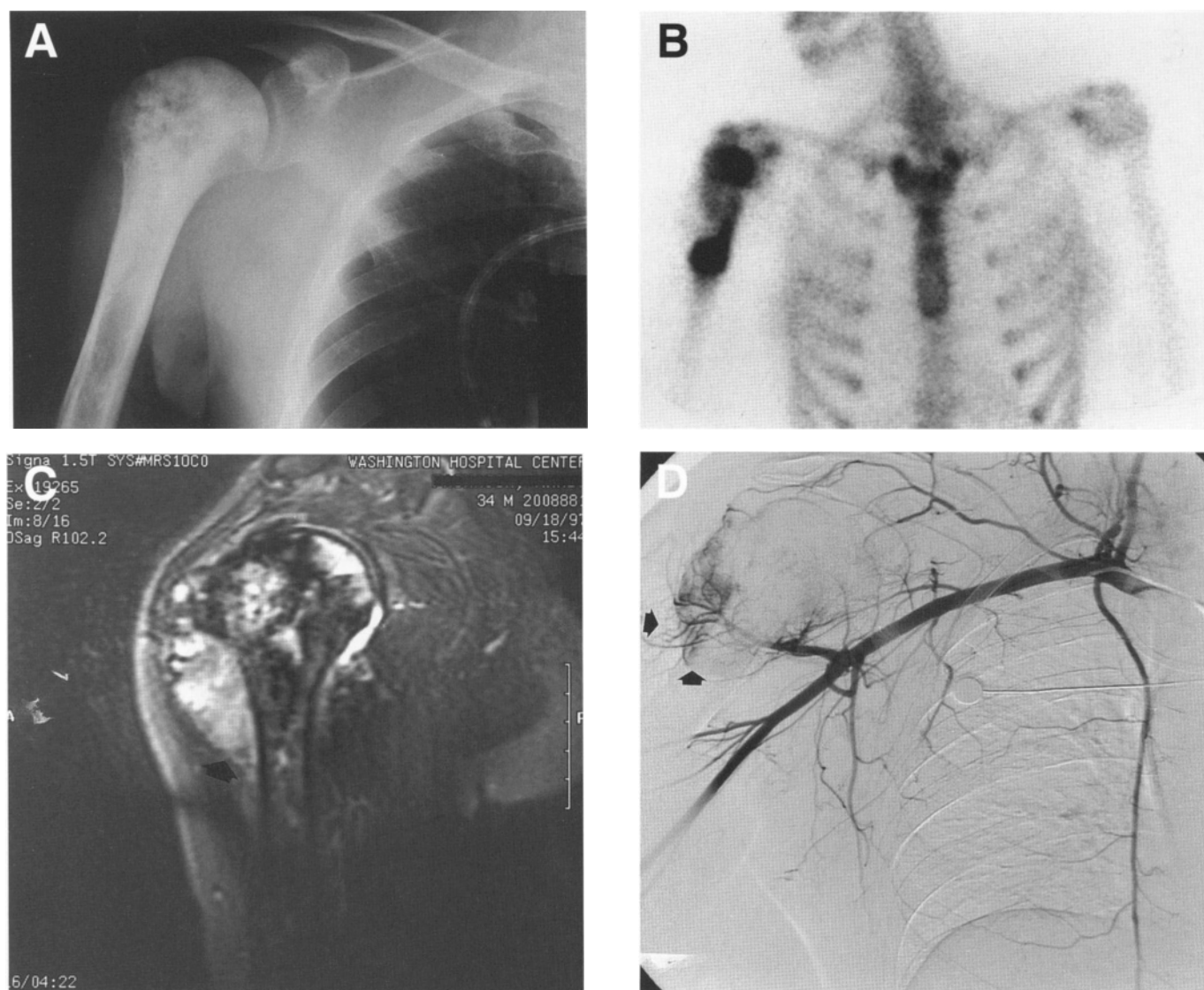


Figure 33.2 (see also following page) Typical case of osteosarcoma of the proximal humerus. (A) Plain radiograph showing a small sclerosing lesion of the proximal one-quarter of the humerus. This is typical of sclerosing osteosarcoma. (B) Bone scan corresponding with (A). (C) MRI of the same patient shows a large extraosseous component extending below the deltoid muscle (arrow). (D) Angiogram following induction chemotherapy showing minimal remaining tumor vascularity. Note that there is some tumor vascularity in the extraosseous component below the deltoid (arrows). There is no tumor vascularity of the main tumor intraosseously. (E) Postoperative radiograph showing the Modular Replacement System, following an extra-articular resection.

risk for local recurrence than those undergoing extra-articular resections. Therefore, it is often necessary to perform an extra-articular resection for high-grade bone sarcomas of the proximal humerus or scapula.

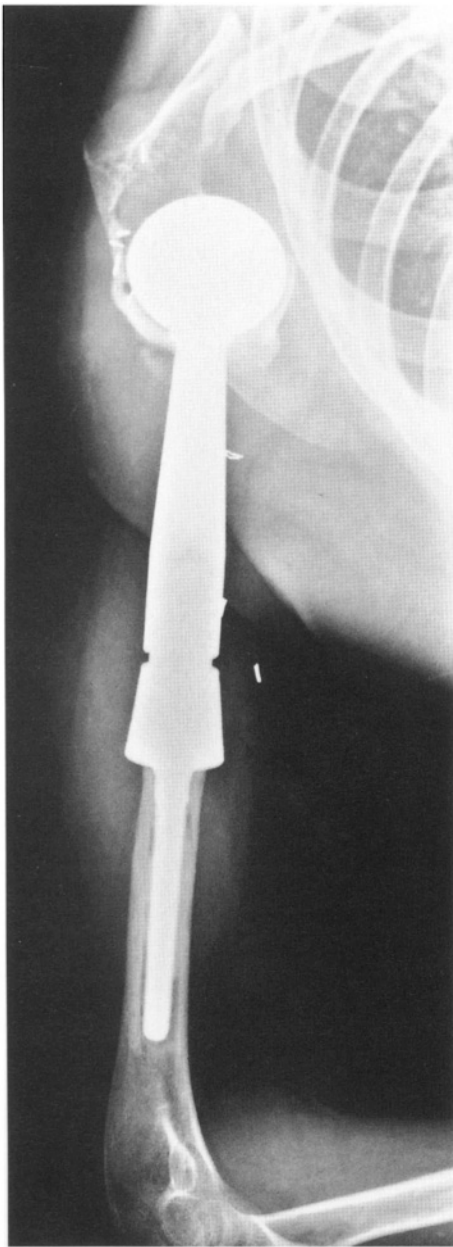
Neurovascular Bundle

The subclavian artery and vein join the cords of the brachial plexus as they pass underneath the clavicle. Beyond this point the nerves and vessels can be con-

sidered as one structure (i.e. the neurovascular bundle). Large tumors involving the upper scapula, clavicle, and proximal humerus may displace the infraclavicular components of the plexus and axillary vessels.

Musculocutaneous and Axillary Nerves

These two nerves are often in close proximity or contact with tumors around the proximal humerus. The musculocutaneous nerve is the first nerve to leave the

E**Figure 33.2 E**

brachial plexus. It typically leaves the lateral cord just distal to the coracoid process, passes through the coracobrachialis, and runs between the brachialis and biceps. Preservation of the musculocutaneous nerve and short head of the biceps muscle is important to ensure normal elbow function. The path of this nerve may vary extensively (within 6–8 cm of the coracoid) and should be identified prior to any resections because it can be easily injured.

The axillary nerve arises from the posterior cord and courses, along with the circumflex vessels, inferior to the distal border of the subscapularis. It then passes

between the teres major and minor to innervate the deltoid muscle posteriorly. Tumors of the proximal humerus are likely to involve the axillary nerve as it passes adjacent to the inferior aspect of the humeral neck, just distal to the joint. Therefore, the axillary nerve and deltoid are almost always sacrificed during proximal humerus resections.

Radial Nerve

The radial nerve comes off the posterior cord of the plexus and continues anterior to the latissimus dorsi and teres major. Just distal to the teres major, the nerve courses into the posterior aspect of the arm to run between the medial and long head of the triceps. Although most sarcomas of the proximal humerus do not involve this nerve, it must be isolated and protected prior to resection.

Axillary and Brachial Arteries

The axillary artery is a continuation of the subclavian artery, and is called the brachial artery after it passes the inferior border of the axilla. The axillary vessels are surrounded by the three cords of the brachial plexus and are tethered to the proximal humerus by the anterior and posterior circumflex vessels. Early ligation of the circumflex vessels is a key maneuver in resection of proximal humeral sarcomas because it allows the entire axillary artery and vein to fall away from the tumor mass. Occasionally, there is anatomic variability in the location of its branches that could lead to difficulty in identification and exploration if not previously recognized. A preoperative angiogram is helpful in determining vascular displacement and anatomic variability.

Final determination of tumor resectability is made at surgery. Early exploration of the neurovascular structures is performed following division of the pectoralis major muscle. This approach does not jeopardize subsequent formation of an anterior flap in patients who require forequarter amputation.

STAGING STUDIES

Appropriate imaging studies are key to successful resections of tumors of the proximal humerus and shoulder girdle. The most useful imaging studies are plain radiography, computed tomography scans (CT), magnetic resonance imaging (MRI), arteriography, and bone scan. Venography is occasionally required.

1. *Computed tomography.* CT is most useful for evaluating cortical bone changes and is considered complementary to MRI in evaluating the chest wall, clavicle, and axilla for tumor extension.



Figure 33.3 Pathologic fracture of a small osteosarcoma of the proximal humerus with minimal displacement. (A) Initial photograph showing minimal displacement of the sarcoma. (B) Three months following induction chemotherapy with Adriamycin, cisplatin, and ifosfamide. (C) Initial CT scan prior to chemotherapy. (D) Postchemotherapy CT scan corresponding to (B); showing complete fracture healing. Limb-sparing surgery can be performed following a pathologic fracture if there is a good response to induction chemotherapy with fracture healing.

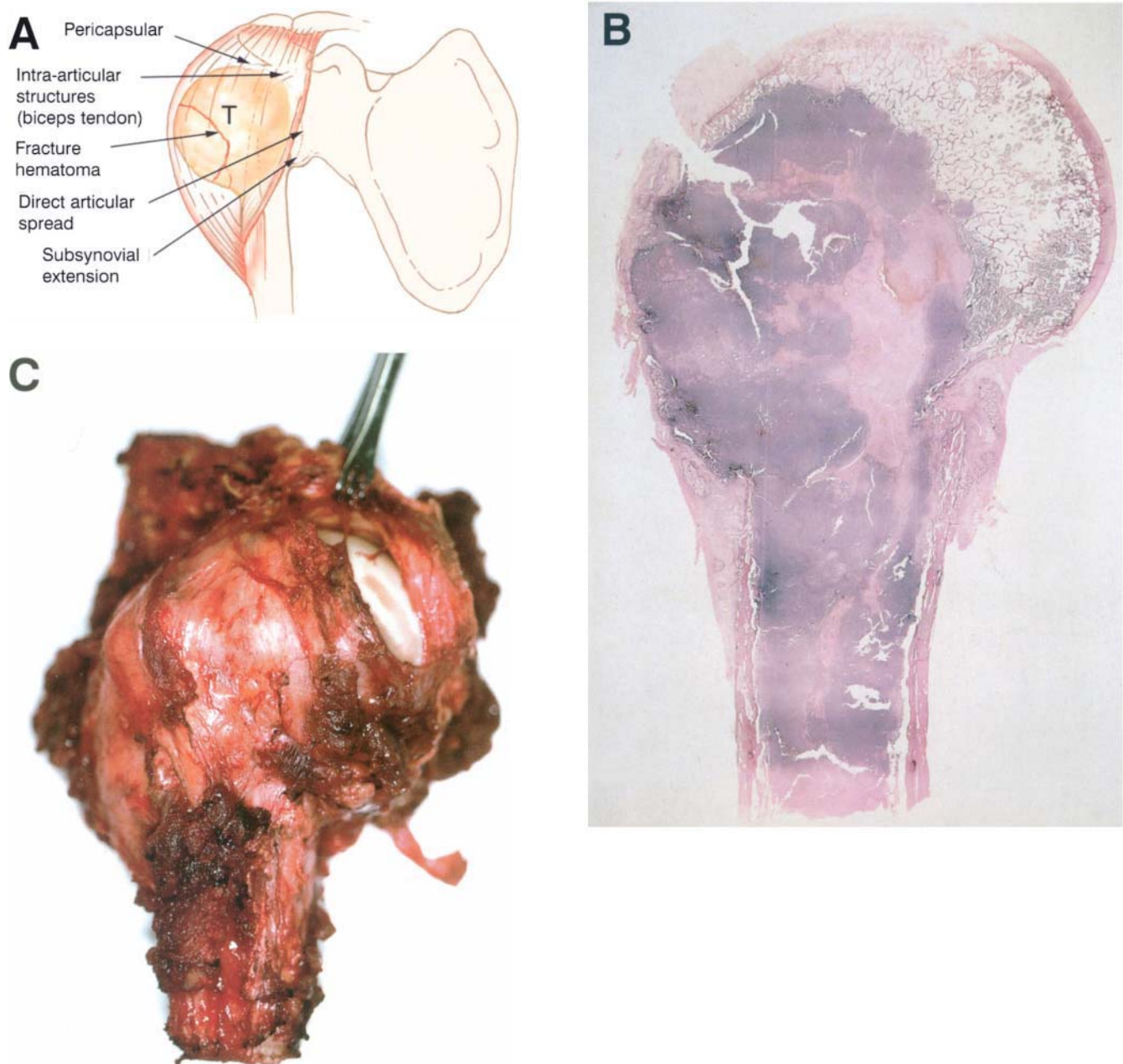


Figure 33.4 (see also following page) Biological and anatomic basis for limb-sparing surgery of the proximal humerus. (A) The mechanisms of extra-articular involvement of tumors of the proximal humerus (see text). Most high-grade tumors of the proximal humerus are treated by an extra-articular (Type V) resection. Mechanisms of intra-articular joint involvement by high-grade tumors of the proximal humerus: there are five mechanisms of tumor spread from the proximal humerus to the glenohumeral joint or capsule. These mechanisms are direct extension through the articular cartilage, along the capsule and synovium, along an intra-articular structure (biceps tendon), through a fracture hematoma. The proximal humerus is at a much higher risk for local recurrence following an intra-articular resection when compared to the local recurrence rate of other major joints. Therefore, it is the author's preference to perform an extra-articular resection for high-grade sarcomas of the proximal humerus (Type V resection). (B) Whole mount of a specimen of a high-grade chondrosarcoma of the proximal humerus. Note the tumor involves the humeral head and shaft with some extraosseous extension. (C) Surgical specimen following an extra-articular resection for a high-grade osteosarcoma. The capsule can be seen to be opened and the humeral head is visualized. This is the typical resection specimen following a limb-sparing procedure for high-grade tumors of the proximal humerus. (D) Gross specimen following a forequarter amputation for a large telangiectatic osteosarcoma of the proximal humerus. There is a huge extraosseous component with massive soft-tissue contamination necessitating an amputation. Today, less than 5% of sarcomas of the proximal humerus require forequarter amputation.

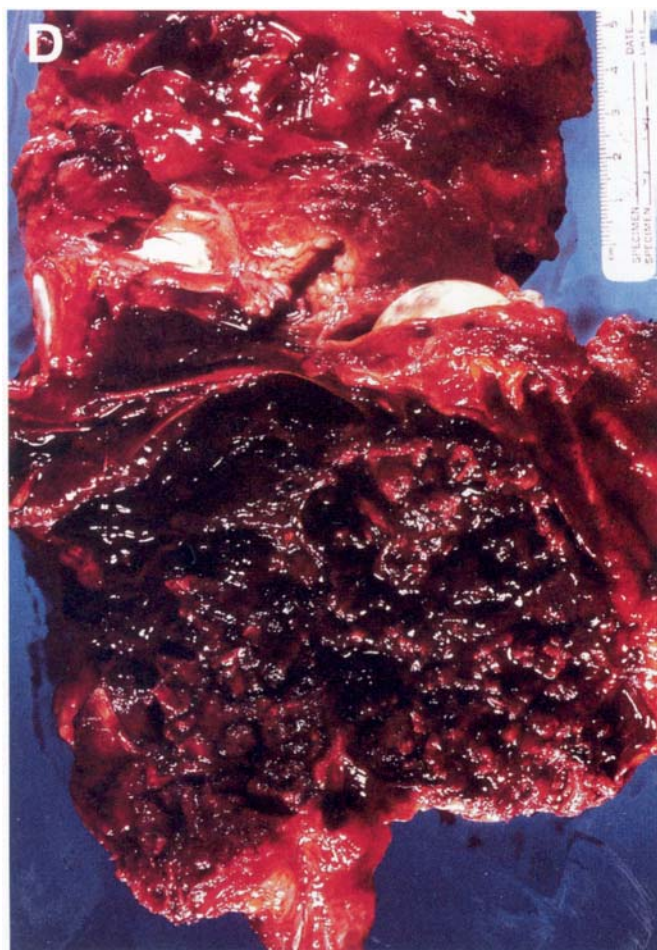


Figure 33.4 D

2. *Magnetic resonance imaging.* MRI is useful to identify intraosseous tumor extent, which is necessary for determining the length of bone resection. It is the best imaging modality for evaluation of soft-tissue tumor involvement, especially around the glenohumeral joint, suprascapular region and chest wall.
3. *Bone scintigraphy.* Bone scintigraphy is used to determine the intraosseous tumor extent and to detect metastases.
4. *Angiography.* Angiography is extremely useful for evaluation of tumor vascularity and tumor response to neoadjuvant chemotherapy. It is also essential for determining the relationship of the brachial vessels to the tumor or the presence of anatomic anomalies. A brachial venogram may also be necessary if there is evidence of distal venous obstruction suggesting a tumor thrombus.

BIOPSY: PROXIMAL HUMERUS

Needle or incisional biopsies of tumors of the proximal humerus should be performed through the anterior

one-third of the deltoid muscle, not through the deltopectoral interval. A biopsy through the anterior one-third of the deltoid results in a limited hematoma that is confined by the deltoid muscle. This portion of the muscle and biopsy hematoma are easily removed at the definitive resection. A biopsy through the deltopectoral interval will contaminate the major pectoralis muscle, which is necessary for reconstruction, increase the risk of hematoma spread along the axillary vessels to the chest wall and make a local resection difficult, if not impossible.

If an open biopsy is required, a short longitudinal incision should be made just lateral to the deltopectoral interval. The dissection should be directly into the deltoid muscle and proximal humerus. The bone should be exposed lateral to the long head of the biceps. No flaps should be developed, and the glenohumeral joint should not be entered.

SURGICAL GUIDELINES

It is important to be extremely familiar with shoulder girdle anatomy and axillary and vascular structures.

1. A utilitarian incision is utilized. The anterior component is an extended deltopectoral incision that exposes the pectoralis major muscle, which is then released and retracted towards the chest wall. This exposes the axillary contents and permits exploration and safe dissection of the vascular structures and infraclavicular plexus.
2. An extra-articular resection is performed. Thus, the axillary nerve is identified and transected. The musculocutaneous nerve is identified and preserved. The radial nerve, which crosses the humerus posteriorly at the level of the deltoid insertion, is preserved.
3. Approximately one-half to two-thirds of the humerus is resected.
4. An extra-articular resection is performed by exposing the glenohumeral joint both anteriorly and posteriorly. The scapula is osteotomized medial to the coracoid along with the distal portion of the clavicle. The resected specimen consists of the proximal one-half of the humerus, the glenohumeral joint, and the distal clavicle en-bloc.
5. A modular replacement proximal humeral prosthesis is utilized to reconstruct the skeletal defect.
6. Attention must be paid to the reconstruction of the muscles for soft-tissue coverage of the prosthesis. Static suspension is performed with Dacron tape and the muscle reconstruction is based upon the pectoralis major being sutured to the remaining scapula. The remaining muscles are then tenodesed

to the pectoralis major muscle. This technique permits immediate stability and restores motor power to the upper extremity.

7. An epineural axillary sheath catheter is utilized to control postoperative pain. A 28-gauge chest tube is used for drainage through a Pleurovac.
8. Postoperatively, only a sling is required for 2 weeks.

ENDOPROSTHETIC REPLACEMENT OF THE PROXIMAL HUMERUS

The Modular Replacement System (MRS), which is used for reconstruction of the shoulder girdle, is shown. The results of the MRS are predictable and successful, and the device is used for both intra- and extra-articular resections.

Endoprosthetic reconstruction following tumor resection entails the following steps (Figure 33.5):

- Fixation of the endoprosthesis in the remaining distal humerus.
- Fixation and stabilization of the prosthetic humeral head to the scapula provide a stable shoulder joint.
- Soft-tissue reconstruction to completely cover the prosthesis and optimize postoperative function.

Dual Suspension Technique

A dual suspension (i.e. static and dynamic) technique is utilized to create shoulder stability. The static reconstruction is as follows: drill holes are made in the distal portion of the osteotomized clavicle and through the remaining scapula at the level of the spine. The head of the prosthesis is secured to the remaining portion of the scapula with a 3 mm Dacron tape so that the prosthesis is suspended mediolaterally (for horizontal stability). It is then suspended, using an additional Dacron tape, in a craniocaudal direction from the end of the clavicle (for vertical stability). The dynamic suspension is provided by transfer of the short head of the biceps muscle to the stump of the clavicle (as described in the next section), that allows elbow flexion.

Soft-tissue Reconstruction

The remaining muscle groups are tenodesed to the pectoralis major and osteotomized border of the scapula with Dacron tape. This mechanism offers dynamic support, assists in the suspension of the prosthesis, and provides soft-tissue coverage. Soft-tissue coverage is essential to cover the prosthesis and prevent skin problems and secondary infections.

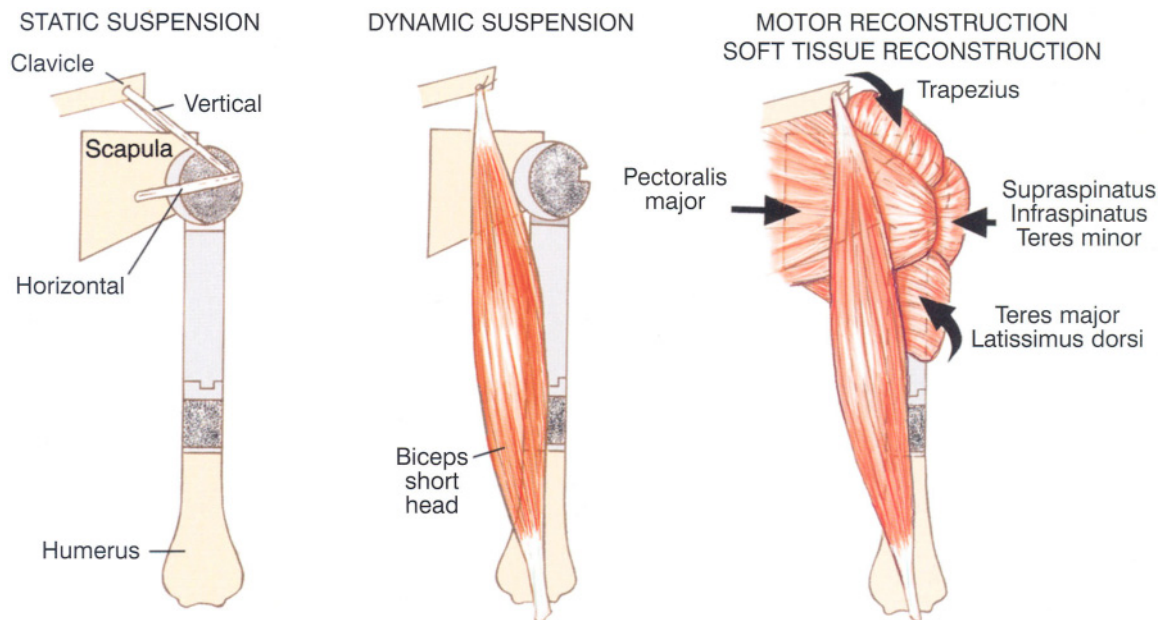


Figure 33.5 Schematic reconstruction of the proximal humerus. There are three major components to the reconstruction of the proximal humerus following an intra- or extra-articular resection. It is important to re-create joint stability and restore muscle power. The author has developed the following techniques of reconstruction (see Figure 33.17):

- Static suspension. The proximal humerus is suspended from the scapula and the clavicle with Dacron tape through drill holes.
- Dynamic suspension is performed by re-creating muscle stability across the new joint. The biceps muscle (conjoin tendon) is transferred to the clavicle. The trapezius is advanced and tenodesed to the pectoralis major muscle.
- Motor reconstruction and soft-tissue coverage. The pectoralis major muscle is sutured to the transected border of the scapula. This covers the prosthesis and re-creates shoulder stability. The trapezius muscle is mobilized and transferred to the pectoralis major muscle in order to regain some lost abduction. The remaining muscles are then tenodesed to the pectoralis major muscle as illustrated. This technique is a reliable method of re-creating shoulder stability and restoring lost motor power. (Seminars in Arthroplasty, Vol 10 No 3 (July) 1999: pp. 142–153)

Extra-articular Resection of the Proximal Humerus (Type V) and Prosthetic Reconstruction

SURGICAL TECHNIQUE

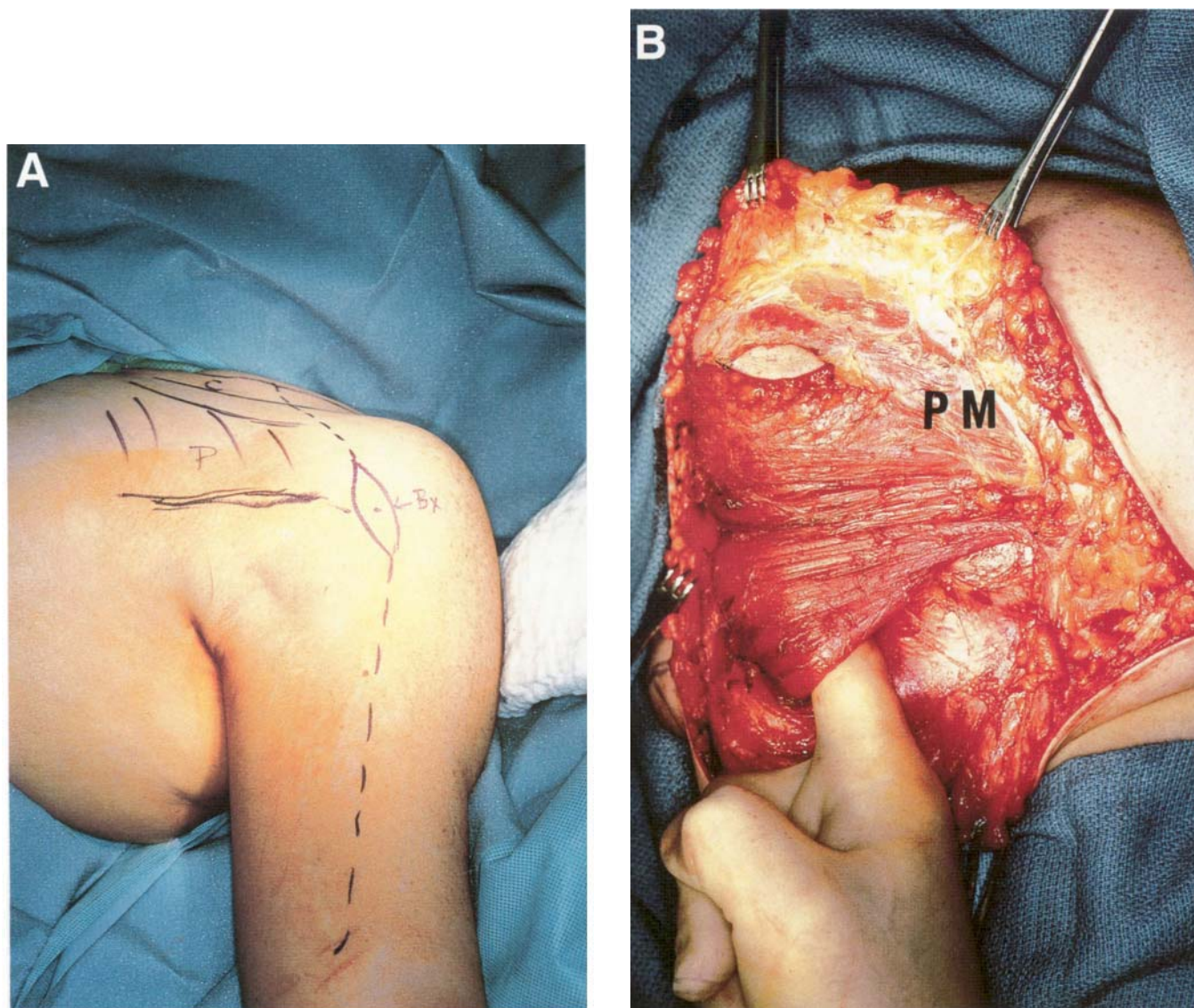


Figure 33.6 (see also following pages) Operative photographs of the exposure of an osteosarcoma of the proximal humerus with a modular replacement reconstruction and multiple muscle transfers. (A) The anterior incision utilized for resection. Note that the biopsy site is ellipsed out. The cross-hatched areas represent the pectoralis major muscle. (B) The deltopectoral interval identified. The biopsy site is seen on top of the deltoid muscle. The surgeon's finger below the pectoralis major (PM) in the axillary space prior to release and mobilization of the muscle. (C) The pectoralis major (PM) has been retracted, exposing the deltoid (D) tumor (T) [proximal humerus covered by the subscapularis muscle] and the neurovascular bundle (arrow) that has been protected by a Penrose drain. The axillary artery and nerves are enclosed with the drain. The subscapularis is now easily visualized (C = coracobrachialis muscle). (D) Photograph showing the surgical defect following resection of the proximal one-half of the humerus. The Penrose drain remains around the vessels. The pectoralis major (PM) is shown reflected. The osteotomized scapular border is seen. The arrow indicates the neurovascular bundle. (E) Posterior exposure prior to extra-articular resection. The deltoid muscle (D) attaches to the spine of the scapula posteriorly. The interval for the scapular osteotomy is identified with pick-ups. (F) Modular prosthetic reconstruction of the surgical defect. The Dacron tape is utilized for suspension (see text). (G) Anterior view of the reconstruction with the modular prosthesis following an extra-articular resection. The Dacron tape is utilized to support the prosthesis and also reattach the pectoralis major muscle (arrow) to the osteotomized section of the scapula to provide for support and coverage of the prosthesis. (H) Multiple muscles are rotated and closed over the surgical defect. (PM) Pectoralis major, (B) biceps, (T) triceps, (TR) trapezius, and (I) infraspinatus.

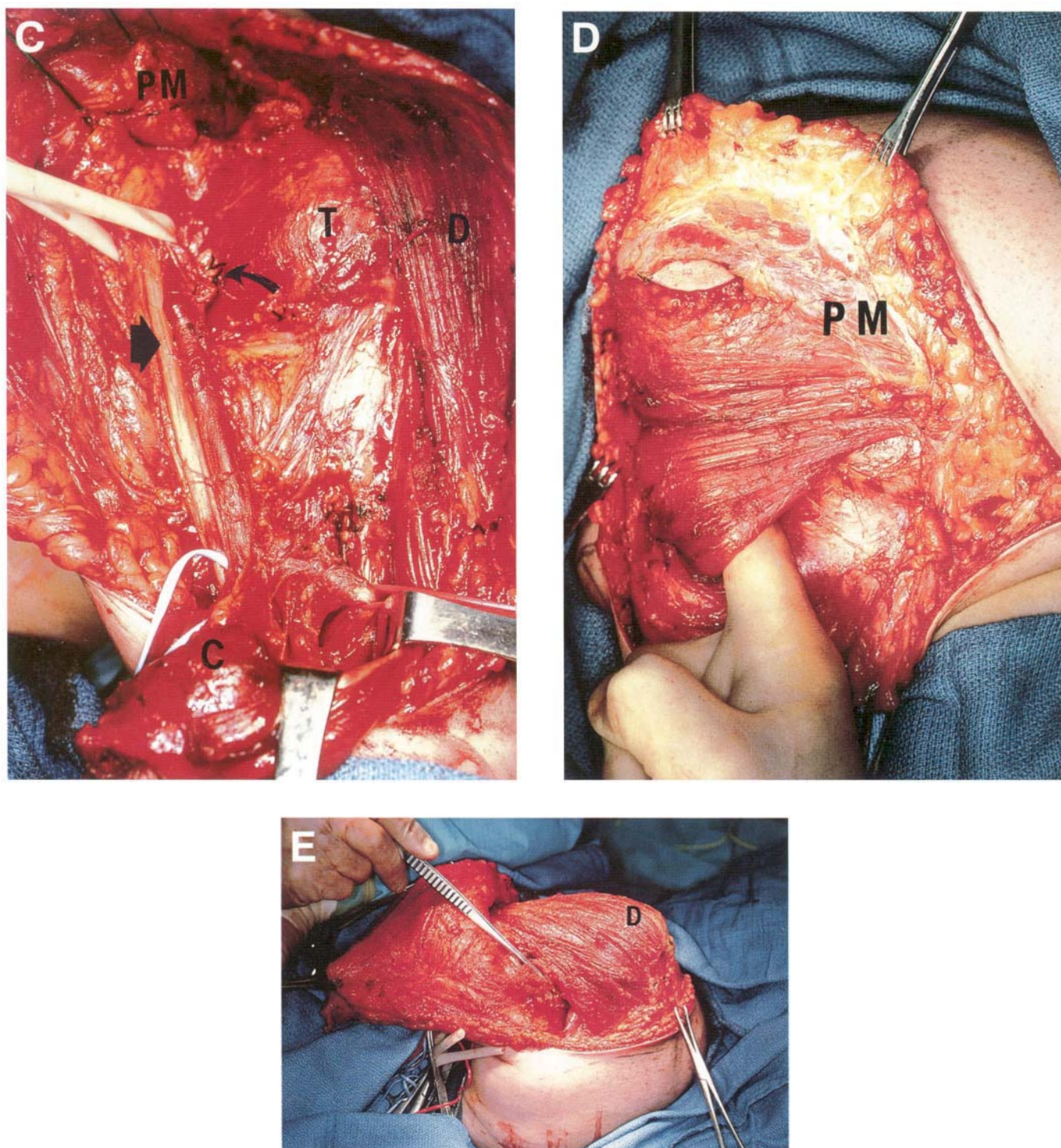


Figure 33.6 C–E Techniques in Shoulder and Elbow Surgery
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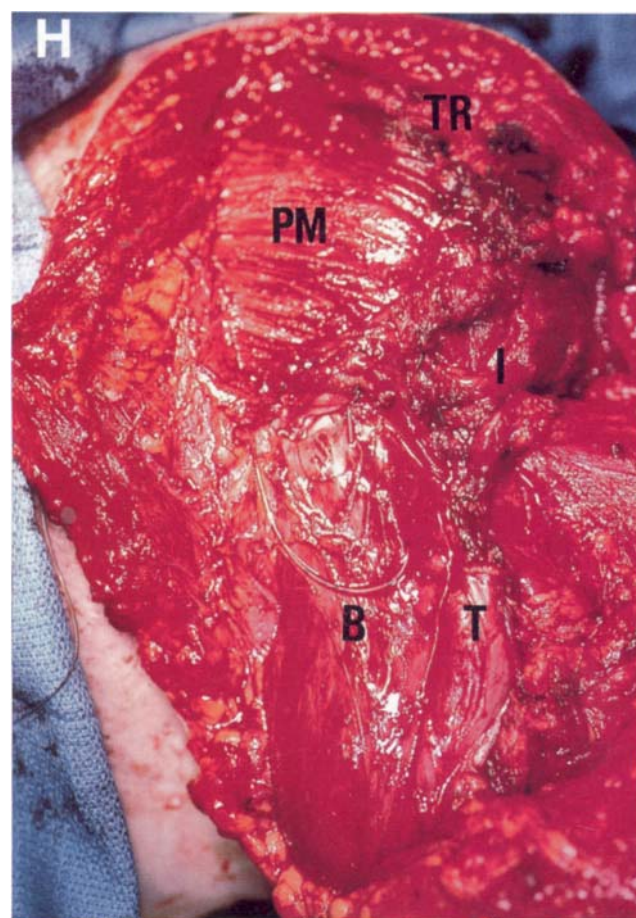
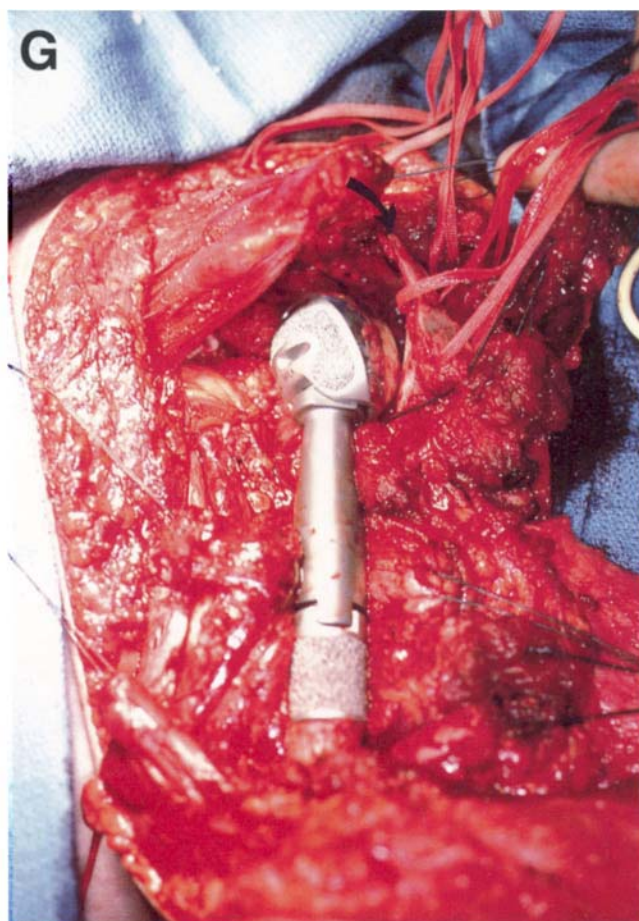
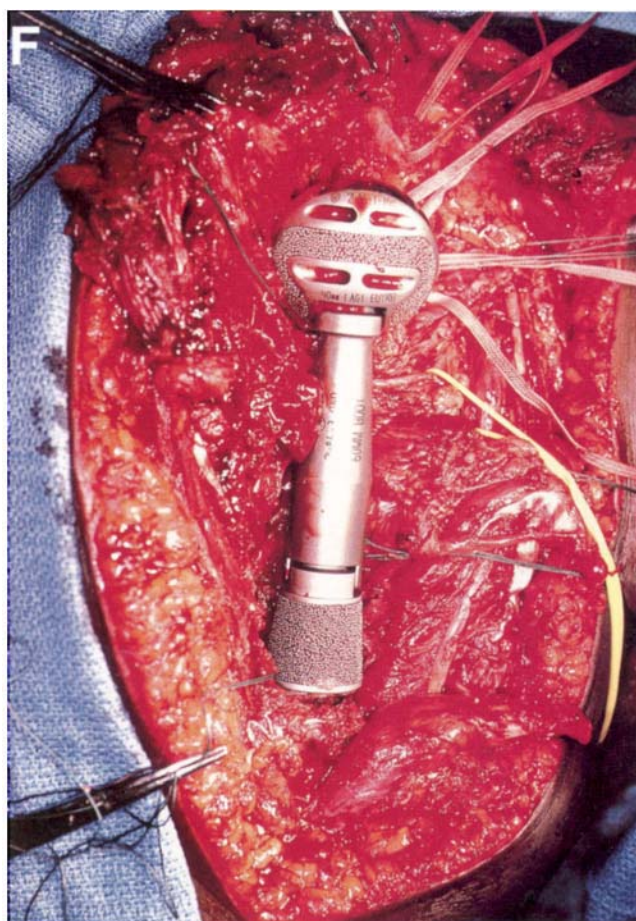


Figure 33.6 F–H

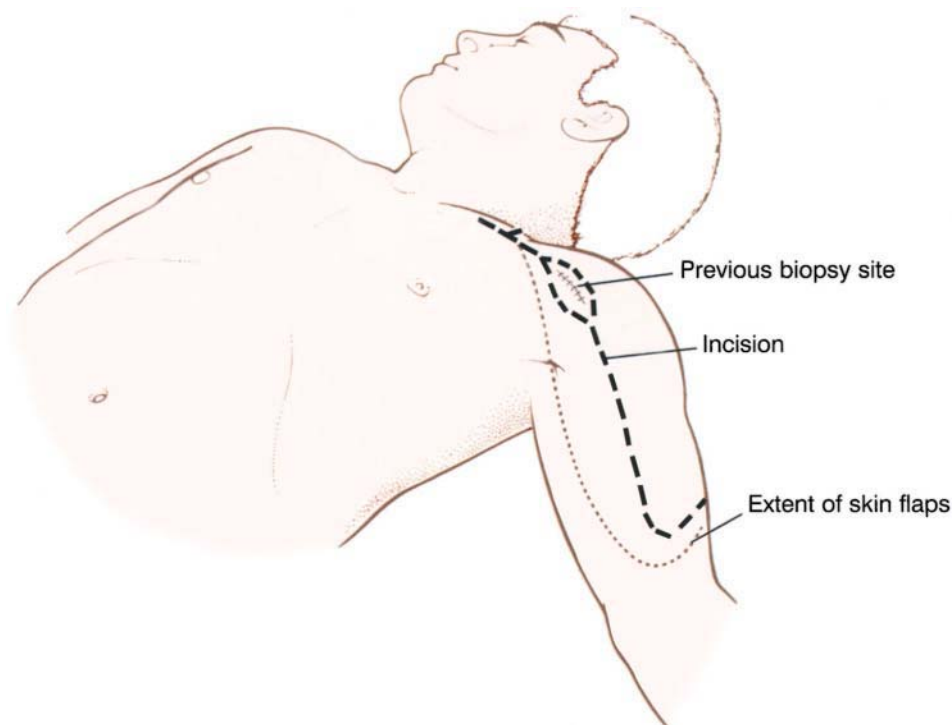
Technique for Type V Shoulder Resection

Figure 33.7 Position and incision. Antibiotics are begun preoperatively and continued until suction drains are removed. The patient is placed in an anterolateral position that allows some mobility of the upper torso. A Foley catheter is placed in the bladder and an intravenous line is secured in the opposite extremity. The skin is prepared down to the level of the operating table, to the umbilicus and cranially past the hairline. The incision starts over the junction of the inner and middle thirds of the clavicle. It continues along the deltopectoral groove and then down the arm over the medial border of the biceps muscle. The biopsy site is excised leaving a 1 cm margin of normal skin. The posterior incision is not opened until the anterior dissection is complete.

Figure 33.8 (see following page) Exploration of the axilla to determine resectability. Anteriorly the skin flap is dissected off the pectoralis major muscle to expose its distal third. This muscle is divided just proximal to its tendinous insertion on the humerus, and the portion of the muscle remaining with the patient is tagged with a suture. The axillary sheath is now identified and the coracoid process visualized. In order to expose the axillary sheath along its full extent, the pectoralis minor, short head of the biceps, and coracobrachialis muscles are divided at their insertion on the coracoid process. All muscles are tagged with a suture for their later identification and use in the reconstruction.

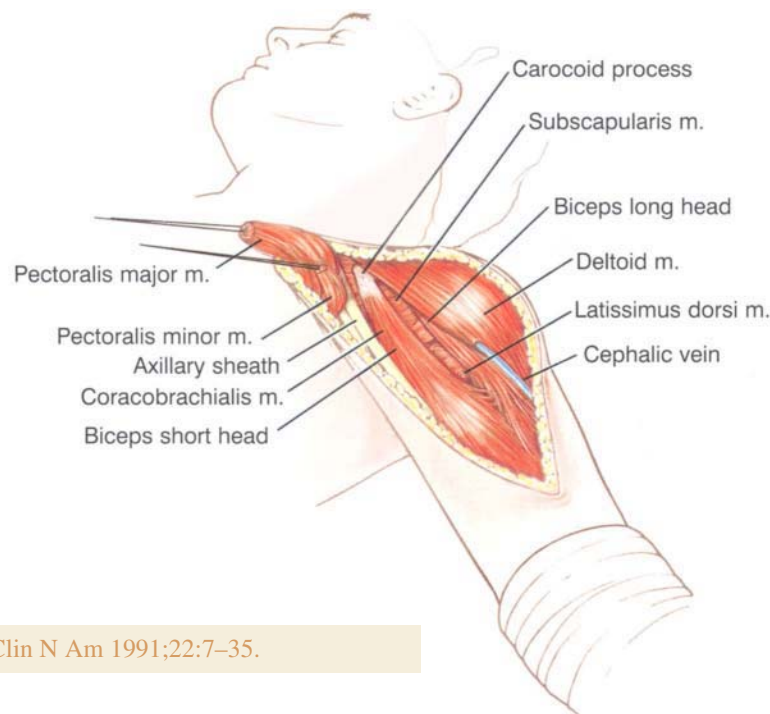


Figure 33.8 Orthop Clin N Am 1991;22:7–35.

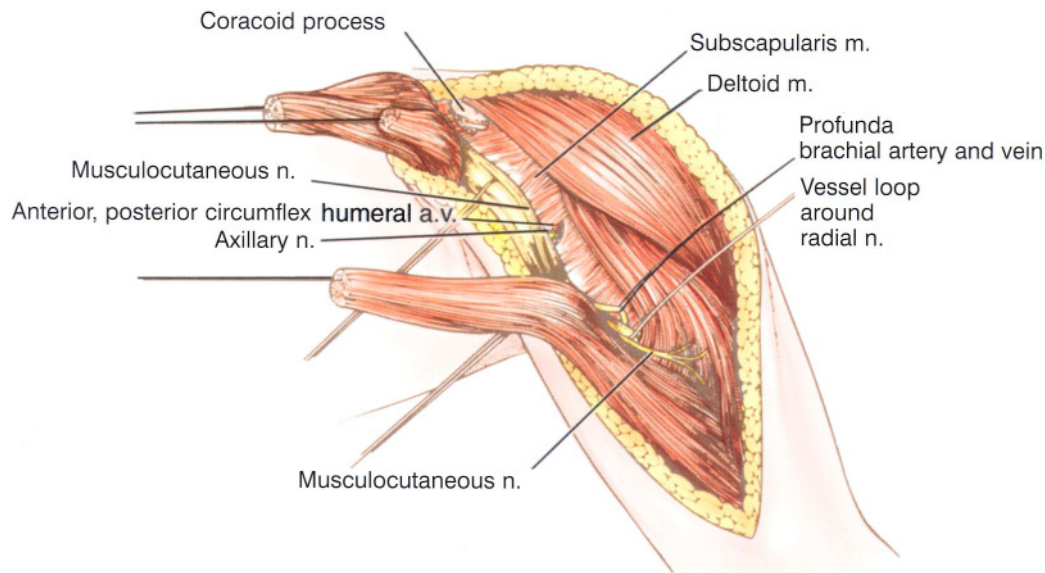


Figure 33.9 Dissection of the neurovascular bundle. Vessel loops are passed around the neurovascular bundle near the proximal and distal ends of the dissection. Medial traction on the neurovascular bundle allows visualization of the axillary nerve, posterior circumflex artery, and anterior circumflex artery. These structures are ligated and then divided. If the neurovascular bundle is found to be free of any extension of the tumor, dissection for the limb salvage procedure proceeds. The musculocutaneous nerve is isolated and carefully preserved. Although sacrifice of this nerve is occasionally required to preserve tumor-free margins of resection. The radial nerve is identified at the lower border of the latissimus dorsi muscle passing around and behind the humerus into the triceps muscle group. The profunda brachial artery that accompanies this nerve may be ligated. The radial nerve passes posterior to the humerus in its midportion (spiral groove). To dissect it free of the bone, a finger is passed around the humerus to bluntly move the nerve away from the bone.

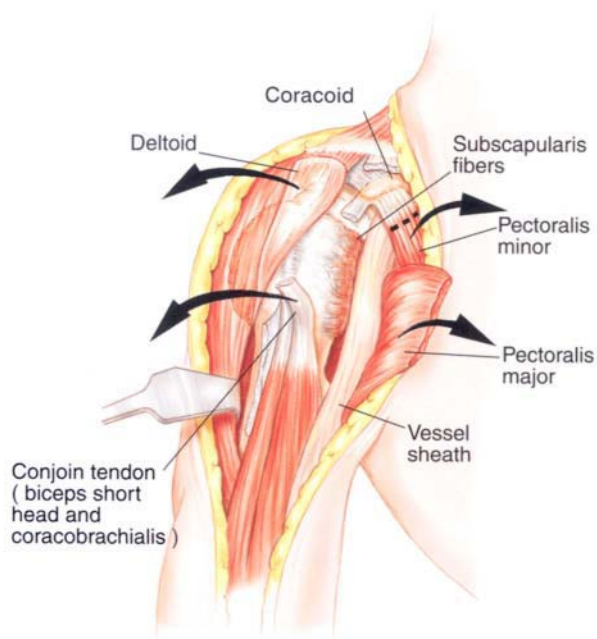


Figure 33.10 Division of muscle groups anteriorly to expose the neck of the scapula. The short and long heads of the biceps are widely separated to expose the humerus. Determine the site for the humeral osteotomy, then transect the long head of the biceps and brachialis muscles at this level. The inferior border of the latissimus dorsi muscle is identified, and a fascial incision is made that allows one to pass a finger behind the latissimus dorsi and teres major muscles several centimeters from their insertion into the humerus. The latissimus dorsi and teres major muscles are transected using electrocautery. External rotation of the humerus exposes the subscapularis muscle, which is transected at the level of the coracoid process. Care must be taken not to enter the joint space. The portions of these muscles that are to remain with the patient are tagged for future reconstruction. By transecting these muscles the anterior portion of the neck of the scapula has been exposed.

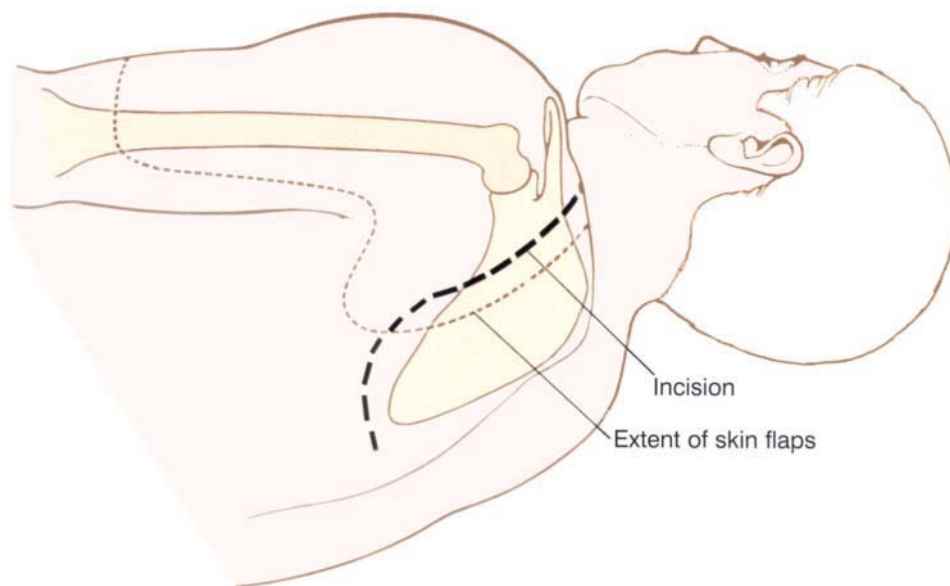


Figure 33.11 Posterior incision and lateral skin flap. The surgeon now changes his orientation from the anterior to the posterior aspect of the patient. Rotation of the table away from the surgeon may allow for better visualization. The posterior incision begins anteriorly over the junction of the middle and lateral thirds of the clavicle. It continues down over the lateral third of the scapula until it passes the lower edge of this bone. A skin flap is developed by dissecting the skin and subcutaneous tissue between the anterior and posterior incisions from the underlying deltoid muscle down to the level of the mid-humerus. If the entire scapula is to be removed, this posterior incision is made longer to allow the skin flap to expose muscle over the entire scapula.

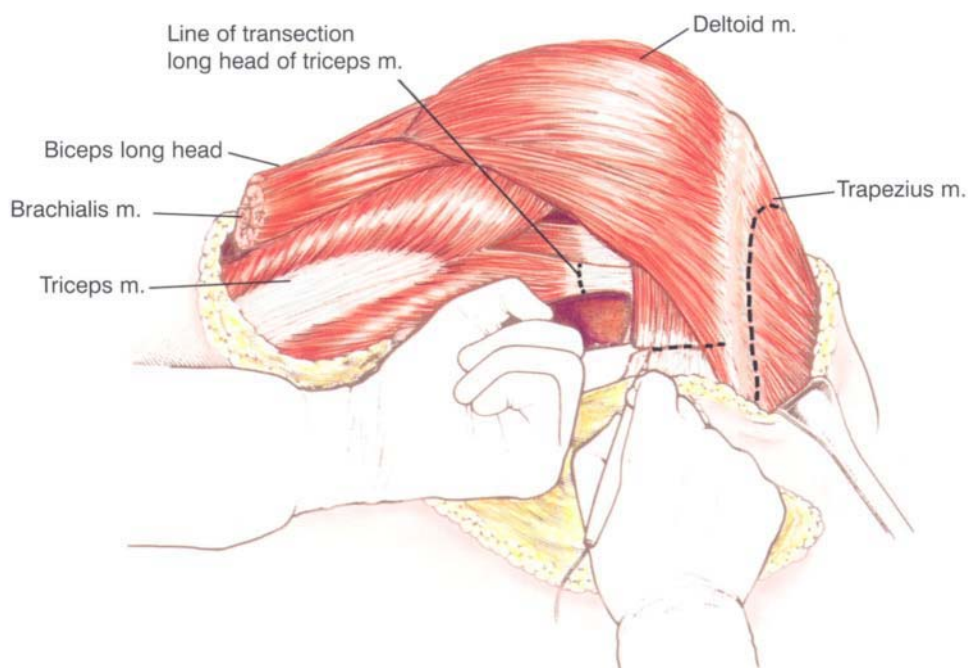


Figure 33.12 Division of muscle groups posteriorly. The thick fascia joining the posterior border of the deltoid muscle to the infraspinatus muscle and scapular spine is divided. The deltoid muscle is left intact as a covering over the tumor mass. The trapezius muscle is transected from its insertion on the scapular spine and acromion. The surgeon's index finger is passed beneath the teres minor up to the area of the planned scapular osteotomy. The supraspinatus, infraspinatus, and teres minor muscles are transected over the neck of the scapula; this allows the plane of transection through the neck of the scapula to be exposed. All transected muscles are tagged proximally. The triceps muscles are transected below their origin from the glenoid. (Techniques in Shoulder and Elbow Surgery Vol 2 No 1 pp. 54–69)

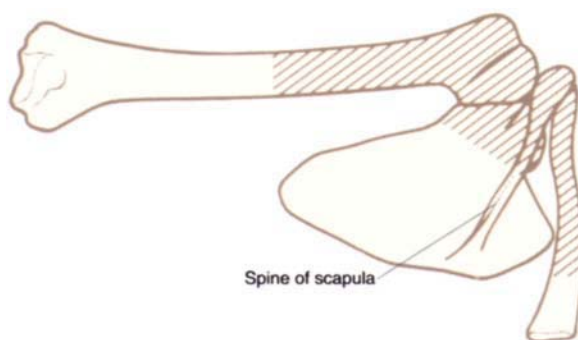


Figure 33.13 Clavicular, scapular, and humeral osteotomies. The clavicle is divided at the junction of its middle and inner one-third. This is usually accomplished with a Gigli saw. The scapula is divided through its surgical neck medial to the coracoid process, also using a Gigli saw. Usually the clavicular and scapular osteotomy are performed prior to the humeral osteotomy.

If the entire scapula is to be resected, the skin flap is raised back to the medial edge of the scapula. After this is accomplished, the rhomboid, levator scapulae and trapezius muscles are divided from their insertions on the scapula. The teres major, teres minor, supraspinatus, infraspinatus and subscapularis muscles need not be divided if a full scapula resection is to be performed.

If the procedure is being performed for a sarcoma of the proximal humerus, the humerus is transected 3–5 cm distal to the tumor as determined by preoperative bone scan. Cryostat sections of tumor margins and touch preparations for cytological examination of the marrow at the site of the osteotomy are obtained. The section of humerus removed is measured and a prosthesis 2–4 cm shorter is selected. Some shortening of the extremity allows better soft-tissue coverage.

Upon removing the specimen, one should note that a generous amount of soft tissue still covers the tumor. The long and lateral heads of the triceps muscle remain on the humerus. The upper portion of the long head of the biceps and the upper portion of the brachialis muscle remain with the specimen. The entire deltoid muscle covers the tumor. The insertions of the supraspinatus, infraspinatus, pectoralis major, latissimus dorsi, teres major, teres minor, and subscapularis muscles remain covering the tumor and constitute the free margins.

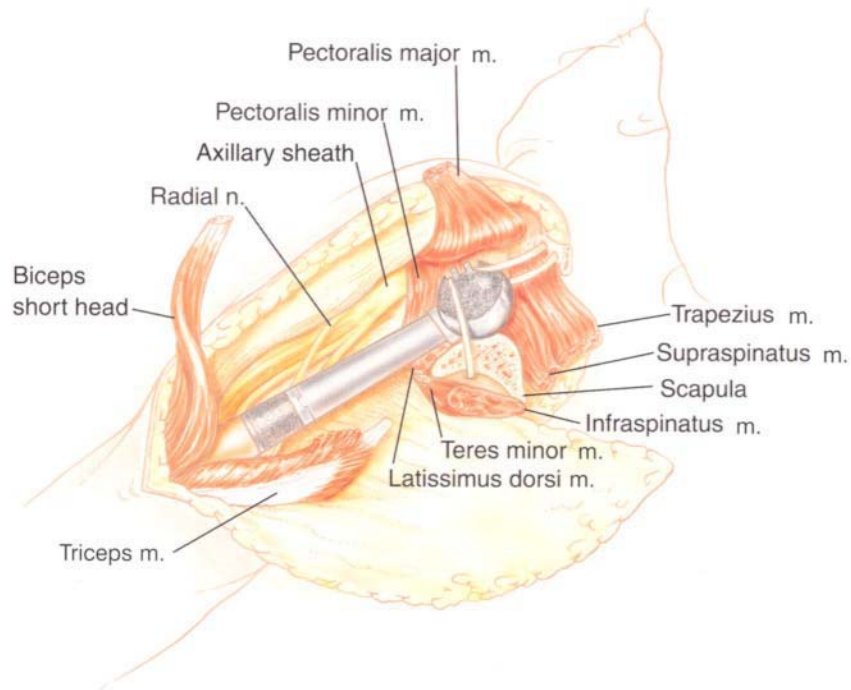


Figure 33.14 Securing the prosthesis. If a prosthesis is to be used, 5–7 cm of distal humerus must be preserved. A power reamer is used to widen the medullary canal of the remaining humerus; it is reamed until it is 1 mm larger than the stem of the prosthesis. The length of the bony specimen is measured so that a prosthesis of appropriate length is used. Methyl methacrylate cement is injected into the medullary canal and the prosthesis is positioned. The head of the prosthesis should be oriented so that it lies anterior to the transected portion of scapula while the arm is in neutral position. The radial nerve should be positioned anterior to the prosthesis so it does not become entrapped between muscle and prosthesis during the reconstruction. Drill holes are made through the scapula at the level of its spine. Drill holes are also made through the distal portion of the transected clavicle. The head of the prosthesis is secured by Dacron tape to the remaining portion of the scapula so that the prosthesis is suspended mediolaterally (horizontal stability). It is suspended in a craniocaudal direction by a second tape from the end of the clavicle (vertical stability). A 3-mm Dacron tape is used. (*Seminars in Arthroplasty*, Vol 10 No 3 (July) 1999: pp. 1422–153)

Figure 33.15 (*see following page*) Reconstruction. The pectoralis minor muscle is sutured to the subscapularis muscle over the neurovascular bundle to protect it from the prosthesis. The pectoralis major muscle is closed over the prosthesis to the cut edge of the scapula and secured with Dacron tape through drill holes. Following this the trapezius, supraspinatus, infraspinatus, and teres minor are secured to the superior and lateral borders of the transected pectoralis major. The teres major and latissimus dorsi muscles are secured to the inferior border of the pectoralis major muscle. The tendinous portion of the short head of the biceps is secured anteriorly under appropriate tension to the remaining clavicle. The long head of the biceps and coracobrachialis muscles are sutured to the short head of the biceps muscle under appropriate tension so that these muscles can work through the short biceps tendon. The remaining triceps muscle is tenodesed to the biceps to cover the lower and lateral portion of the shaft of the prosthesis. Ideally when the proximal and distal muscular reconstruction is complete the prosthesis is covered in its entirety by muscle. (*Seminars in Arthroplasty*, Vol 10 No 3 (July) 1999: pp. 142–153)

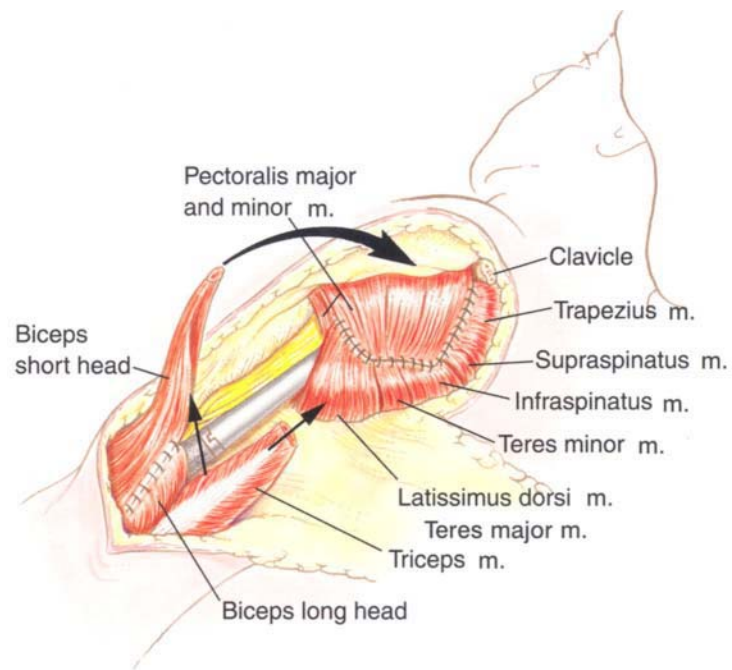


Figure 33.15

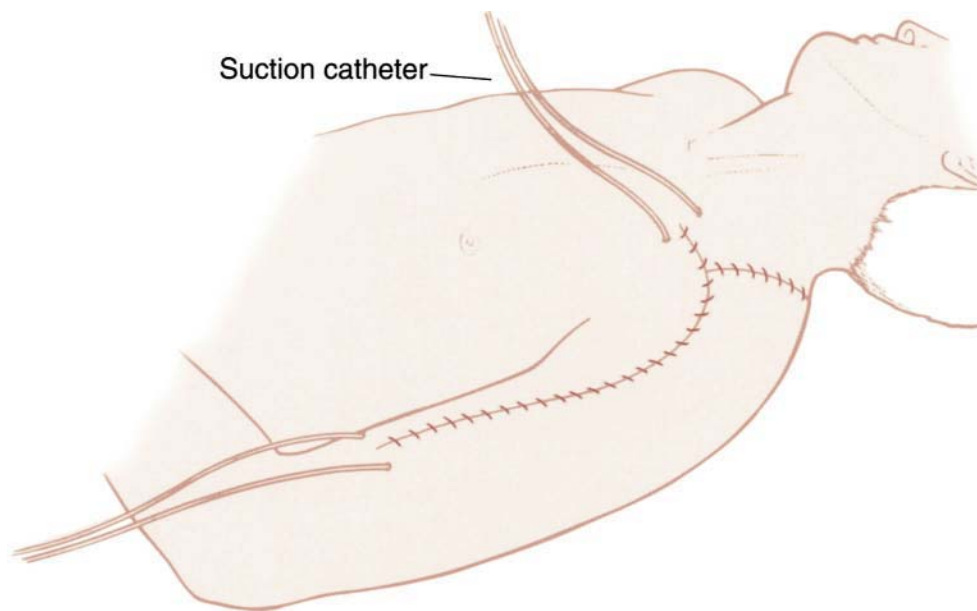


Figure 33.16 Closure. Large-bore suction catheter drainage is secured. The superficial fascia is closed with absorbable suture and the skin is closed with clips. Povidiodine ointment is applied to the incision along with a dry sterile dressing. A sling and swathe are applied in the operating room.

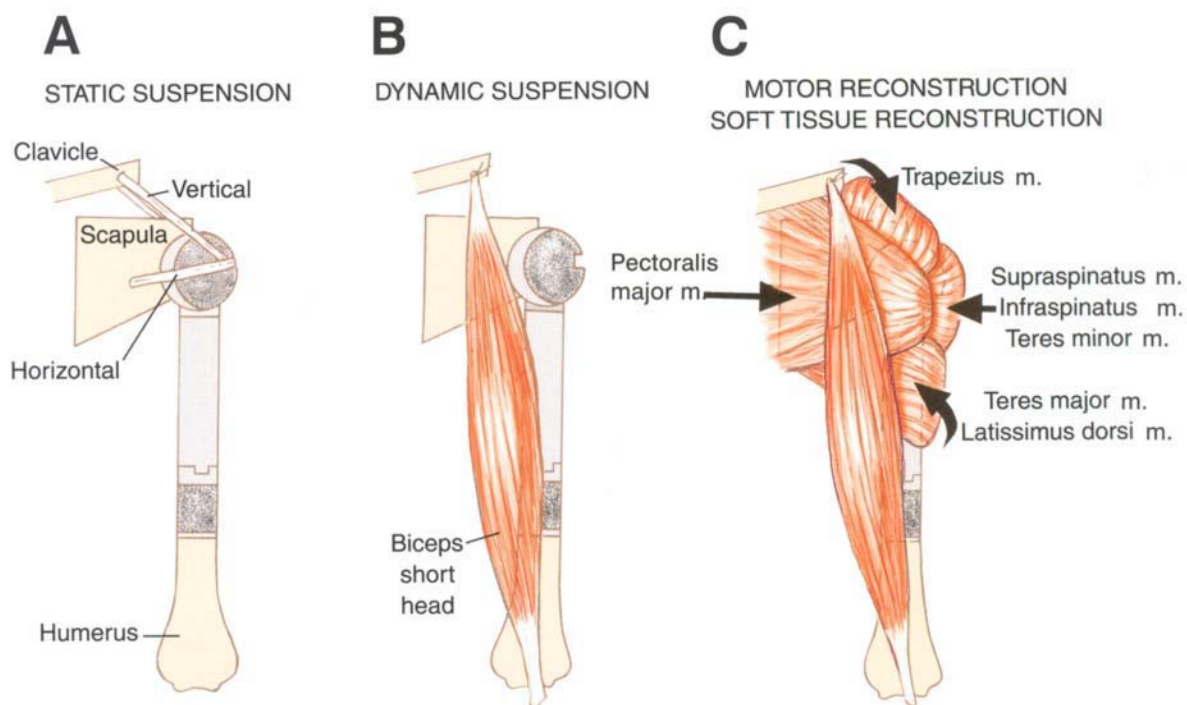


Figure 33.17 (A) Static suspension of the prosthesis. The interposition prosthesis is secured horizontally by Dacron tape placed through drill holes in the scapula. Vertical stability is achieved by passing tape through drill holes in the end of the clavicle. (B) Dynamic suspension of the prosthesis. Elbow flexion is preserved by transferring the short head of the biceps muscle to the end of the clavicle. (C) Motor reconstruction and soft-tissue coverage. The pectoralis major muscle is secured to the scapula to provide forward flexion of the shoulder. Extension of the shoulder occurs through transfer of the trapezius, teres major, and latissimus dorsi muscles. (Seminars in Arthroplasty Vol 10 No 3 (July) 1999: pp. 142–153)

Figure 33.18 (see following page) Intraoperative photographs of an intra-articular resection of the proximal humerus with reconstruction using a Gore-Tex® graft (Type IA resection). (A) Intraoperative defect following resection of a large renal cell carcinoma of the proximal humerus. The axillary nerve and deltoid muscle must be preserved if an intra-articular resection is to be performed (small arrow shows axillary nerve; note its course around the glenoid (G), entering the deltoid posteriorly; D shows the deltoid muscle). The pectoralis major (P) has been detached and retracted, exposing the axillary vessels and nerves. The neurovascular bundle (large arrows) must be carefully dissected away from the large soft-tissue component of the tumor prior to resection. It is essential to preserve the musculocutaneous nerve (me) as well as the radial nerve (R) and the axillary nerve (small arrow). Exposure is facilitated by detaching the pectoralis major and reflecting it toward the chest wall. The pectoralis minor and the conjoin tendon must be released from the coracoid. The neurovascular sheath is found in the loose axillary fat and is dissected. (B) Gross specimen following resection. Note the extraosseous tumor component (large arrow) which is typical of renal cell carcinoma metastases to the bone. The proximal humerus is a common site for metastatic renal cell carcinomas. (C) Capsular reconstruction with Gore-Tex® graft. Note the proximity of the neurovascular structures. The Gore-Tex® is first sutured to the remaining glenoid labrum with Dacron tape. (D) The humeral head of the prosthesis is then inserted into the Gore-Tex® (new capsule) (GX) and held closely to the glenoid and then it is sutured to the holes in the prosthesis with Dacron tape. The remaining capsule is sutured to the Gore-Tex® "capsule". The redundant Gore-Tex® is then trimmed and sutured with Ethibond sutures (curved arrows) to close the new pseudocapsule. We utilize Gore-Tex® reconstruction even if there are remaining capsular structures. This reinforces the capsule and rotator cuff and prevents subluxation and dislocation.

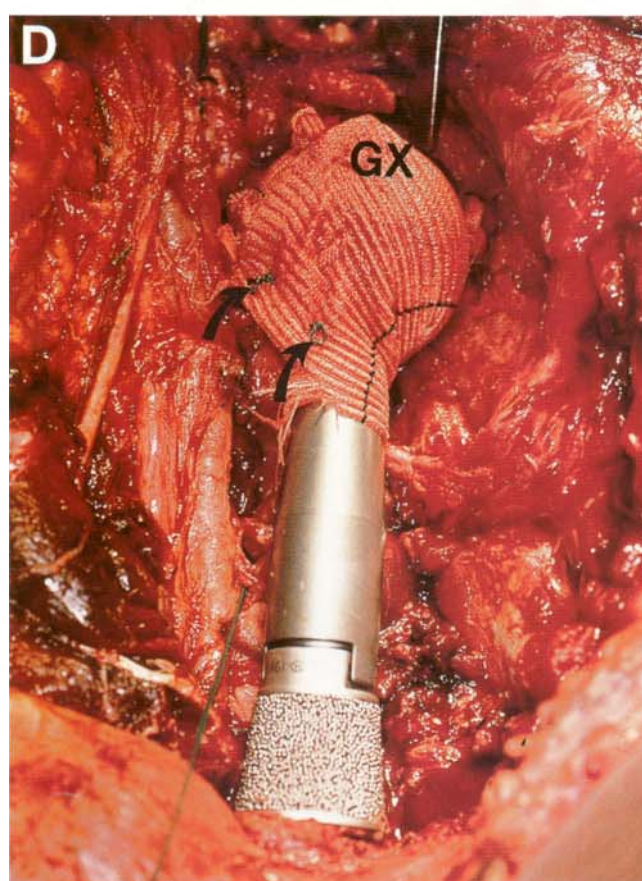
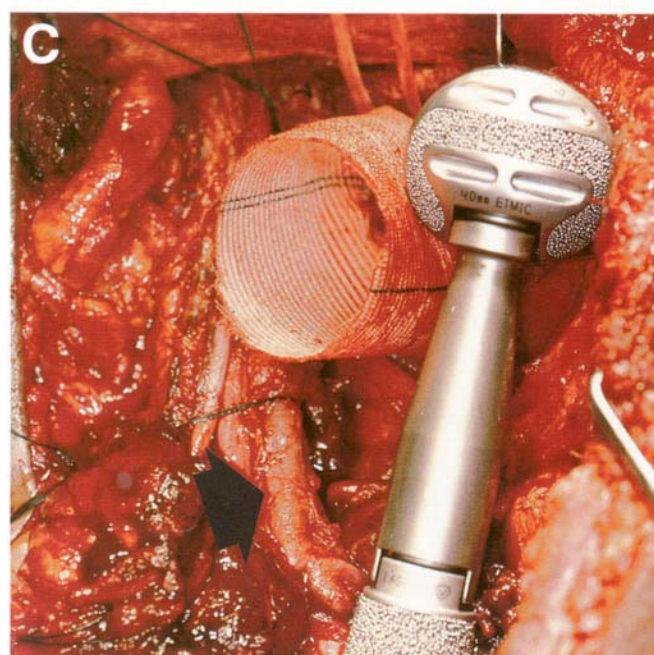
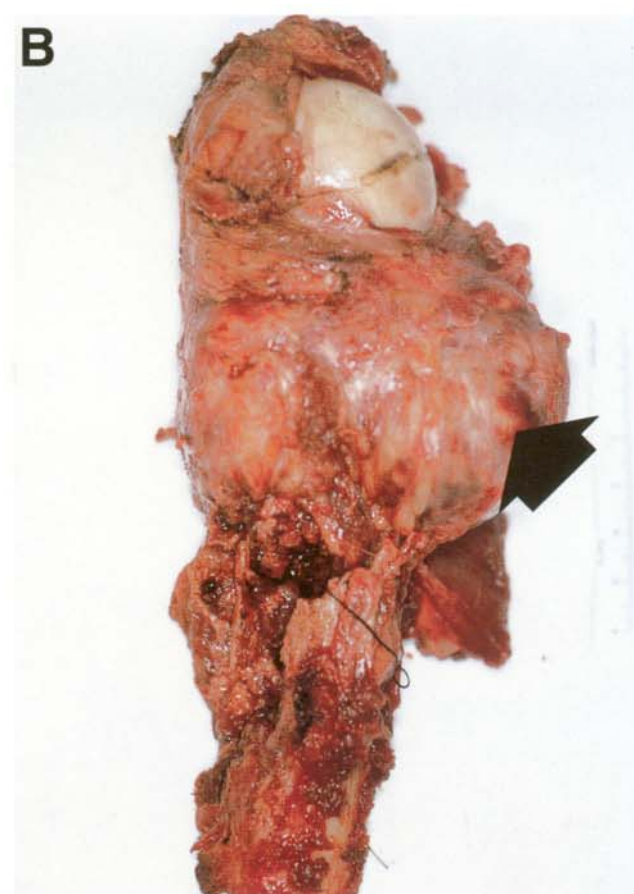
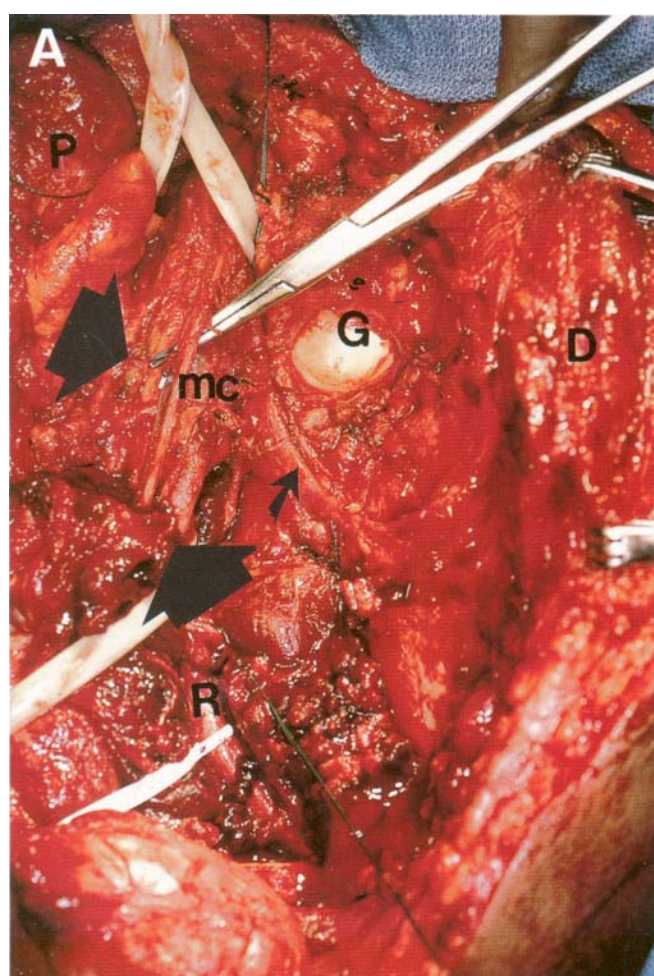


Figure 33.18 A–D

Type I Resection

Intra-articular resection of the proximal humerus is indicated for low-grade sarcomas or high-grade sarcomas confined to the bone without extraosseous extension (Stage IIA). The abductor mechanism and axillary nerve are usually preserved. This procedure is not recommended for high-grade sarcomas with soft-tissue extension. The prosthesis is suspended from the glenoid with Gore-Tex[™] graft that is reinforced by any remaining capsule (Figure 33.18).

- Anterior utilitarian shoulder incision is not required. The posterior component is not used.
- The axillary nerve is explored early and preserved. If there is tumor extension to the nerve, then the procedure is converted to a Type V resection.

- The humeral prosthesis is suspended from the glenoid labrum with 32 mm Gore-Tex. The remaining capsule is sutured to the new Gort-Tex capsule. This

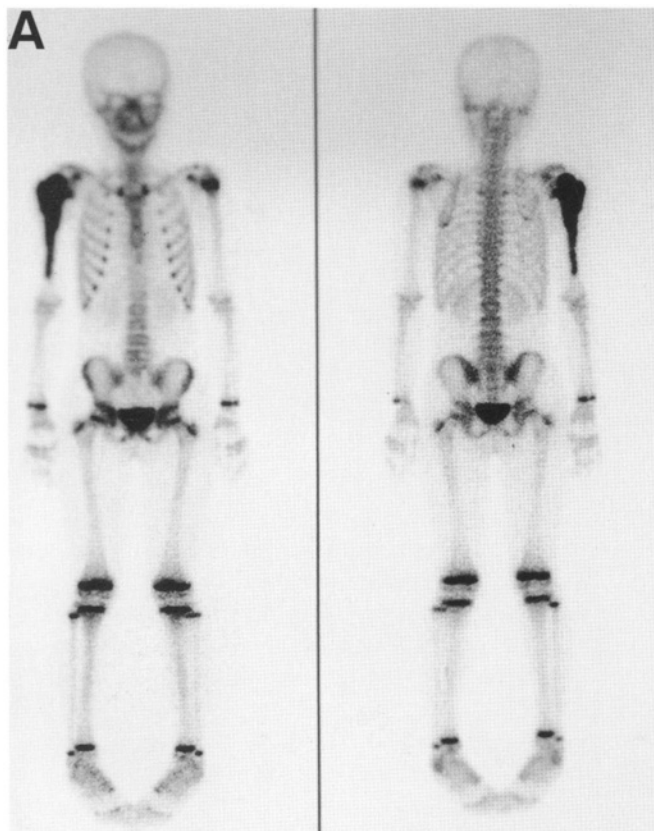


Figure 33.19 (see also following page) Osteosarcoma involving almost the entire humerus, necessitating a total humeral replacement as a limb-sparing procedure in lieu of a forequarter amputation. (A) Bone scan showing 90% of the humerus is involved by a high-grade osteosarcoma. (B) Plain radiograph following induction chemotherapy showing a large extraosseous osteosarcoma of the proximal humerus with a soft-tissue component that has ossified secondary to chemotherapy. Note the reossification of the tumor, which was unexpected in the distal humerus, just above the elbow (arrow.) (C) Plain radiograph of a total humeral replacement following a Type V shoulder girdle resection combined with a distal humeral resection. Note a fixed hinge prosthesis was utilized. (D) Composite photograph of a total humeral resection with a large proximal soft-tissue component reconstructed with an expandable prosthesis due to the patient's immature skeleton. Either an articulated or non-articulated elbow component can be utilized depending on the patient's age. It is important to reconstruct the elbow capsule and tenodesse the muscles to the capsule if a non-hinged prosthesis is utilized. (Orthopedic Clinics of North America Vol 22 No 1 January 1991)

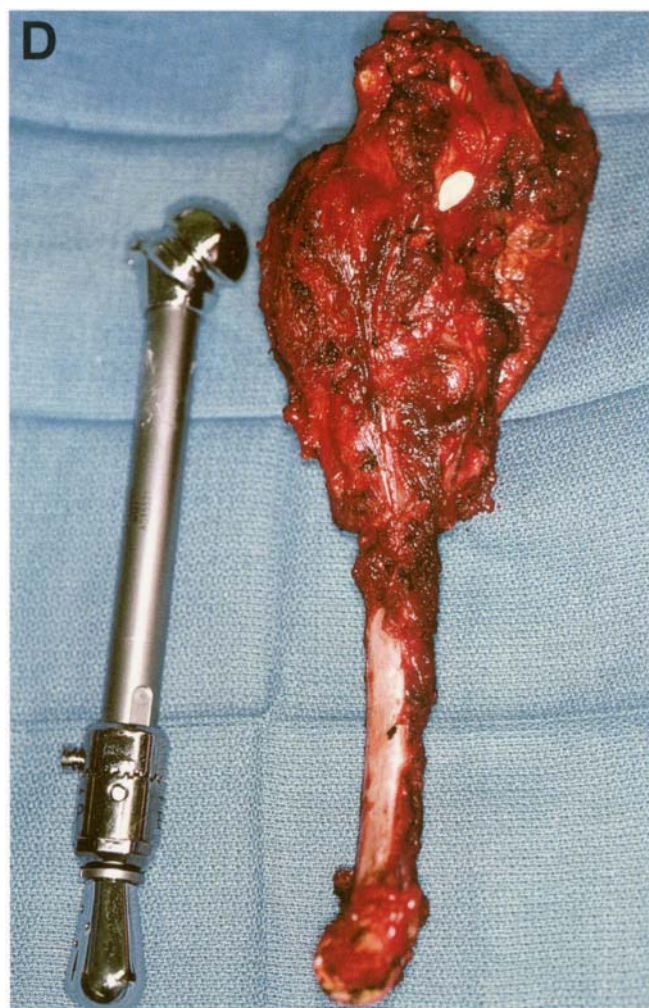
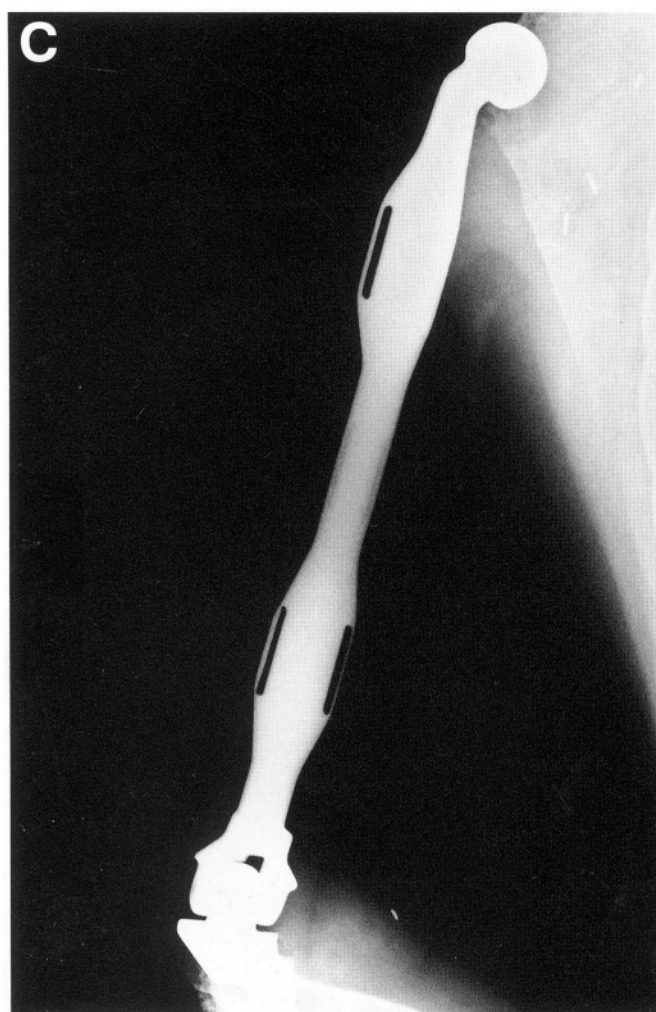


Figure 33.19 C,D

avoids glenohumeral joint subluxation and dislocation.

Total Humeral Resection and Prosthetic Reconstruction

Total humeral replacement is unusual but is indicated when there is tumor involvement of a large portion of the diaphysis, such as in Ewing's sarcoma, or when an extremely short segment of distal humerus remains following adequate tumor resection. The surgical technique is a combination of that used for the proximal humerus and distal humerus resections. Reconstruction provides stability of both shoulder and elbow joints (Figure 33.19).

Exposure and Extension of Type V Procedure

The surgical approach is similar to that used for a Type V resection (i.e. anterior utilitarian approach) but requires additional distal exposure and identification and mobilization of the brachial artery and vein and

the radial, ulnar, and median nerves (Figure 33.20). The incision and exposure are continued down the antero-medial aspect of the arm, across the antecubital fossa and, if necessary, down the anterior aspect of the forearm. The brachial vessels, along with the median and ulnar nerves, are identified medially in the arm. The medial intermuscular septum is transected to allow further dissection and mobilization of the ulnar nerve so that it can be retracted medially with the brachial vessels and median nerve. The biceps is retracted medially with the neurovascular bundle. The radial nerve is identified and passes around the humerus and into the interval between the brachialis and brachioradialis, and continues into the forearm.

The pronator teres and common flexor origins are transected medially, and the brachioradialis, extensor carpi radialis longus, and common extensor origins are released laterally to expose the distal humerus. A small cuff of muscle is left around the tumor as needed. The medial triceps muscle is usually resected with the tumor, but the lateral and long heads are retained. The

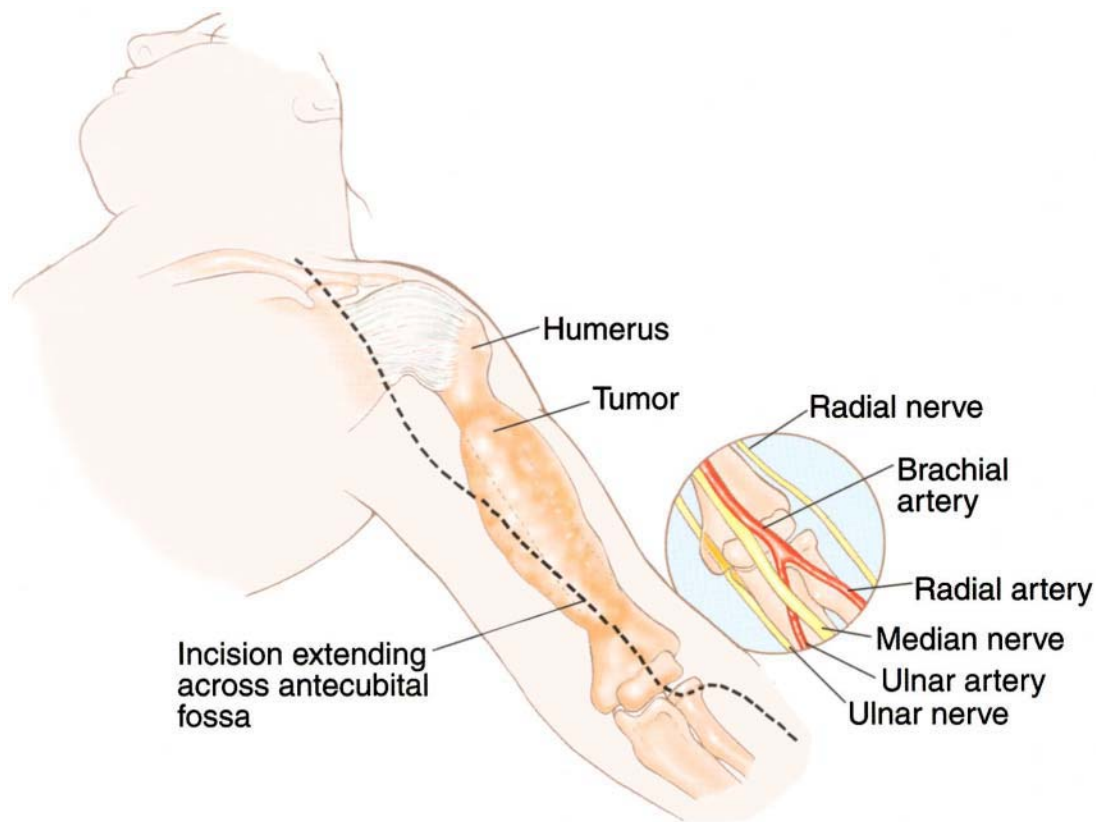


Figure 33.20 Schematic diagram of a total humeral resection. The resection of the proximal 90% of the humerus is similar to the Type V resection seen in [Figure 33.18](#). The incision is extended along the elbow joint anteriorly and the brachial vessels, ulnar nerve, and median nerve are identified and retracted. The shoulder is then reconstructed proximally. The elbow joint is either an articulating or non-articulating prosthesis based on the patient's age. It is essential to reconstruct the capsule and the adjacent muscles to the elbow joint for stability. A posterior splint is utilized postoperatively for 2–3 weeks to allow for stability.

triceps tendon is kept attached to the olecranon. The olecranon is not osteotomized. The elbow joint is opened anteriorly and the capsule released circumferentially. The humeroulnar and radiohumeral joints are then disarticulated.

Prosthetic Reconstruction

Reconstruction of the total humerus is similar to that of the proximal humerus. Distally, an ulnar endoprosthetic component with an intramedullary stem is cemented, with the olecranon left intact. Several articulating elbow devices are available.

Muscle Reconstruction

The reconstruction technique is similar to that used for the proximal humerus, with the addition of distal soft-

tissue and joint capsule reconstruction. The brachioradialis, pronator teres, and flexor carpi radialis muscles are sutured to the remaining biceps and triceps muscles to secure soft tissue around the flared distal portion of the humeral endoprosthesis. The remaining muscles are closed in layers in an attempt to cover the entire prosthesis.

Postoperative Management

A posterior splint is used to protect the elbow reconstruction for 7–10 days. The surgical incision and wounds are examined on the fourth to fifth postoperative day.

DISCUSSION

High-grade sarcomas of the shoulder girdle have been treated traditionally by interscapulothoracic amputation.

Non-ablative extirpation has been rare. This chapter contains a complete description of the technique for a modified Tikhoff–Linberg procedure in patients with sarcomas of the proximal humerus. Also, modifications of the procedure for tumors at other anatomic sites have been utilized. Proximal humeral lesions require resection of about two-thirds of the humerus.

The technique of resection and reconstruction requires a thorough knowledge of the regional anatomy and technique of musculoskeletal reconstruction. Essential aspects of the treatment plan should be emphasized. The initial biopsy should be performed through the anterior portion of the deltoid muscle for a lesion of the proximal humerus. The deltopectoral interval should not be utilized, because biopsy here would contaminate the deltopectoral fascia, the subscapularis, and pectoralis major muscles, and would jeopardize the ability to perform an adequate resection through uninvolved tissue planes. For the definitive resection the initial incision extends along the medial aspect of the biceps muscle, divides the pectoralis major and exposes the neurovascular structures, thereby enabling the surgeon to determine resectability early in the dissection. This incision does not jeopardize construction of an anterior skin flap in patients who will require forequarter amputation.

The length of bone resection is determined preoperatively from a bone scan and MRI. To avoid a positive margin at the site of humeral transection the distal osteotomy is performed 3–5 cm distal to the area of abnormality on the scan. Segmental reconstruction of the resultant humeral defect is necessary to create shoulder stability. The authors do not leave a flail extremity. Reconstruction is necessary to maintain length of the arm and to create a fulcrum for elbow flexion. We recommend a custom or modular prosthesis. Alternatively, other surgeons utilize autografts (usually fibulas) or allografts as spacers in obtaining an arthrodesis. We do not recommend osteoarticular allografts or intra-articular resections for high-grade bone sarcomas; those techniques were developed during the 1960s and 1970s. Superior results are routinely obtained with modular prosthetic replacements combined with reconstruction of the soft tissues. The key to success is reconstruction of the stability of the joint and soft-tissue coverage of the prosthesis.

AXILLARY TUMORS

Introduction

Several types of malignant tumors may involve the axillary space and may require surgical resection. Primary sarcomas occur within the muscles (pectoralis major, latissimus dorsi, teres major, and subscapularis

muscles) that make up the borders of the axillary space. Rarely do they develop within the axillary fat itself. More commonly, large metastatic deposits to the regional lymph nodes create large, matted masses that may require resection. The most common of these are metastatic melanoma and recurrent breast carcinoma. In addition, there are primary tumors that arise from the brachial plexus, and the axillary vessels, such as leiomyosarcomas of the axillary vein and neurofibrosarcomas of the adjacent nerves. Large tumors of the proximal humerus or scapula often extend into the axillary space and require the same imaging evaluation and surgical approach.

The key to adequate and safe surgical resection of axillary tumors is the complete visualization and mobilization of the infraclavicular portion of the brachial plexus; the axillary artery, vein and the cords that surround them. In general, imaging studies of the axillary space are not reliable in determining vascular or nerve sheath involvement. Multiple imaging studies are required (Figures 33.21–33.23), but the decision to proceed with a limb-sparing surgery is based on the intraoperative findings at the time of exploration.

Gross tumor involvement of the brachial plexus and/or the major vessels is an indication for amputation or for the need to abandon the attempted resection. Other contraindications to axillary tumor resection include involvement of the adjacent chest wall. The technique of axillary space exploration via the transpectoralis approach described here has been developed by the authors, and has been found to be the most useful in exploring the tumor, determining resectability, and performing a safe resection.

Unique Anatomic Considerations

Anatomic Borders

The axilla is a pyramid-shaped space between the chest wall and the arm. The apex of the pyramid superiorly is formed by the junction of the clavicle and the first rib. This apex is approximately 1–2 cm medial to the coracoid process. The anterior wall of the axilla is formed by the pectoralis major muscle, and the posterior wall is formed by the subscapularis, teres major, and latissimus dorsi muscles. The chest wall and the serratus anterior muscle form the medial wall of the triangle. The humeral shaft covered by the muscle fibers of the coracobrachialis and the short head of the biceps define the lateral wall. The axilla is triangle-shaped when seen from both the coronal and axial views.

The most significant structures of the axillary space are the axillary artery and vein, which are surrounded by the cords of the brachial plexus as they enter from the apex and pass through the axillary space medial to

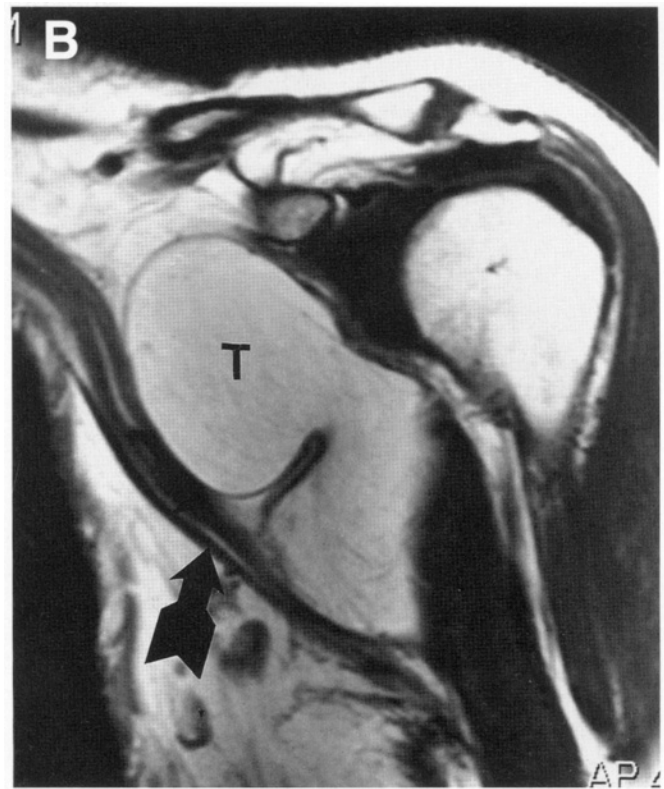
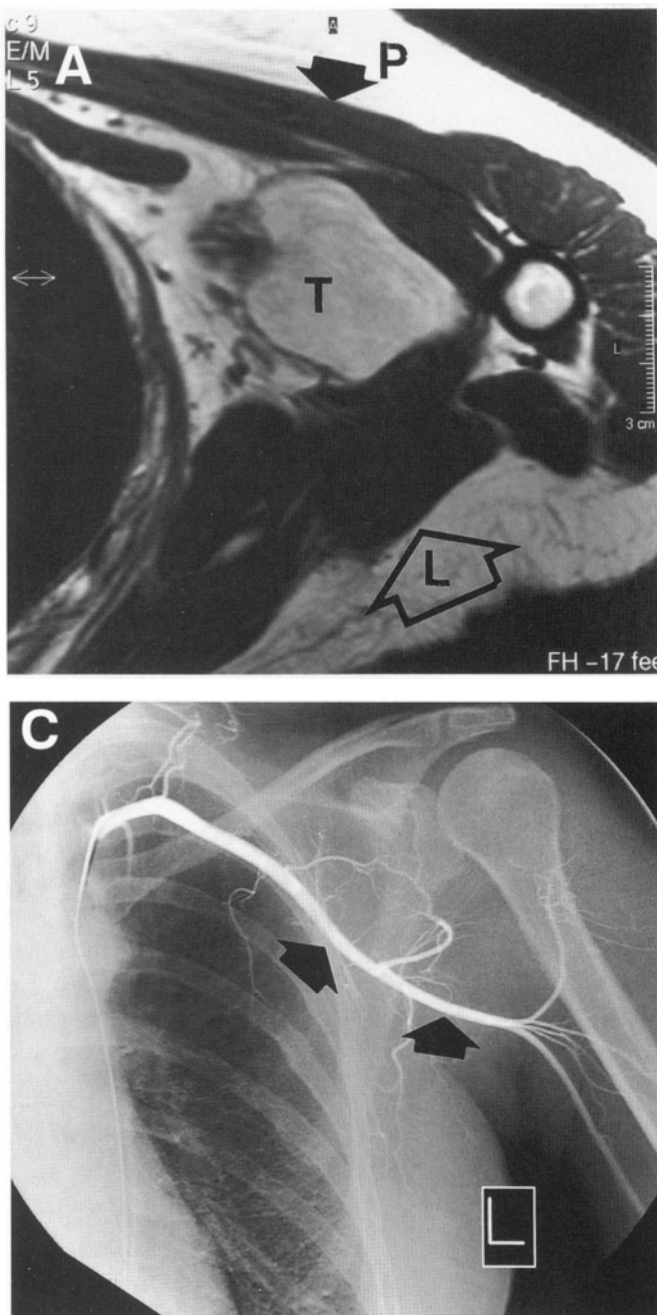


Figure 33.21 Liposarcoma (low grade) of the axillary space. (A) MRI of the left axilla demonstrates a large tumor (T) filling the axillary space. The axillary space is formed by the pectoralis major muscle (P) anteriorly; the latissimus dorsi (L) and the teres major muscles form the posterior border. This is a good demonstration of a primary tumor arising within the axillary space. (B) Coronal MRI. This T1-weighted image demonstrates the tumor (T) filling up the entire axillary space from proximal to the coracoid process (level 1) to the inferior margin. The neurovascular sheath (solid arrow) is displaced inferiorly. (C) AP angiogram corresponding to the coronal MRI demonstrates marked displacement of the axillary artery (arrows). This is an early arterial phase and demonstrates minimal vascularity.

the coracoid to the medial aspect of the humeral shaft. This space is filled with a fair amount of fat. The lymphatics and lymph nodes follow the axillary vessels. The space is bounded anteriorly by the deep clavi-pectoral fascia that arises from the clavicle and covers the deep fat below the pectoralis major muscle. Inferiorly, the fascia wraps around the base of the axilla.

It is extremely important that the surgeon identify this layer before entering the deeper layers.

Pectoralis Major and Conjoined Tendon Muscles

There are two major muscles that form the gateway to the axillary space and that lie just below the clavi-pectoral fascia. These are the pectoralis minor muscle

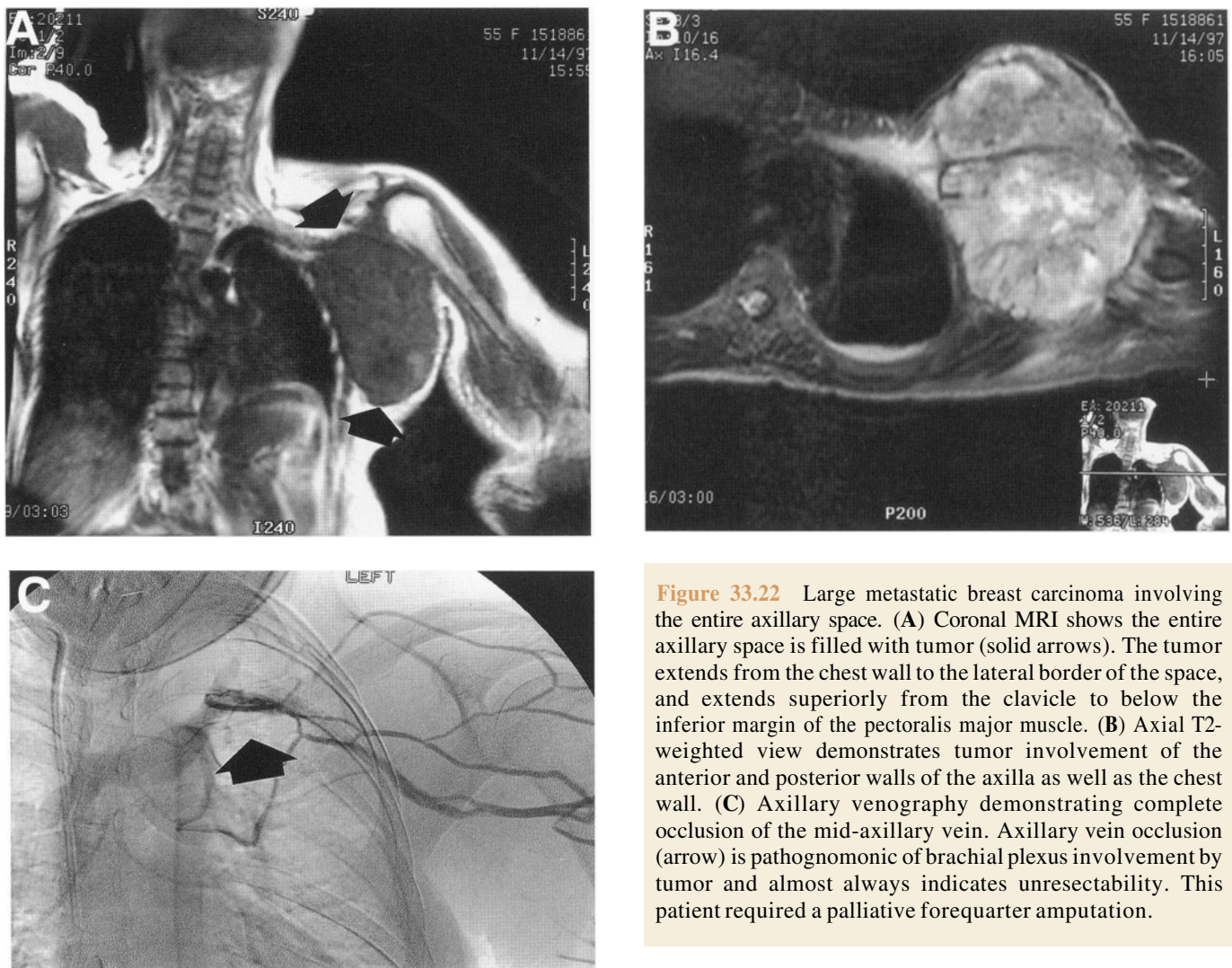


Figure 33.22 Large metastatic breast carcinoma involving the entire axillary space. (A) Coronal MRI shows the entire axillary space is filled with tumor (solid arrows). The tumor extends from the chest wall to the lateral border of the space, and extends superiorly from the clavicle to below the inferior margin of the pectoralis major muscle. (B) Axial T2-weighted view demonstrates tumor involvement of the anterior and posterior walls of the axilla as well as the chest wall. (C) Axillary venography demonstrating complete occlusion of the mid-axillary vein. Axillary vein occlusion (arrow) is pathognomonic of brachial plexus involvement by tumor and almost always indicates unresectability. This patient required a palliative forequarter amputation.

(arises from the chest wall and attaches to the coracoid) and the conjoined tendon (arises from the coracobrachialis and short head of the biceps along the medial aspect of the humerus). These two muscles must be identified in the clavi-pectoral fascia during the surgery. This identification is the key to accurate identification and dissection of all structures that are located more deeply within the axillary fat.

Infraclavicular Brachial Plexus

The infraclavicular portion of the brachial plexus is the most significant anatomic component involved in surgery in the axillary region; therefore it must be

thoroughly evaluated and its anatomy must be completely understood. The axillary artery and vein are contained within a single sheath and are surrounded by the cords of the infraclavicular plexus. The lateral, posterior, and medial cords of the plexus are found at the level of the pectoralis minor muscle. At the lower border of the pectoralis minor muscle these cords give rise to the five major nerves of the extremity: median, ulnar, radial, musculocutaneous, and axillary nerves.

The lateral cord gives rise to the musculocutaneous nerve, which travels along the medial aspect of the conjoined tendon and enters into the muscle belly of the coracobrachialis and then into the short head of the

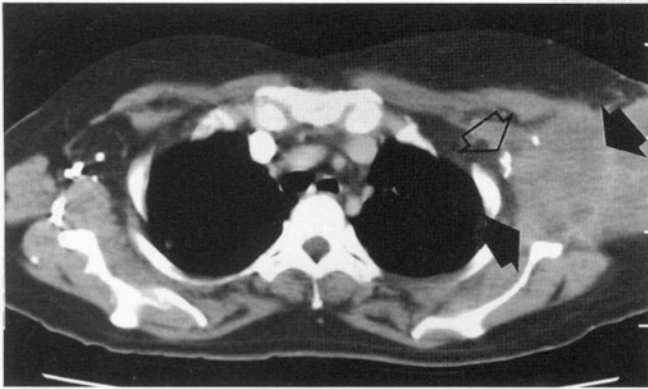


Figure 33.23 CT scan shows a large metastatic melanoma filling the axillary space. The tumor (solid arrows) involves the subscapularis muscle posteriorly and the pectoralis major muscle anteriorly. The axillary vessels are seen displaced (open arrow). CT and MRI are extremely useful in determining the bony and soft-tissue involvement and extension, respectively, into the axillary space.

biceps. This nerve is the first to be identified during the exploration. It is located in the superficial axillary fat inferior to the coracoid process. The posterior cord gives rise to the axillary nerve, which travels deep in the space and passes inferior to the glenohumeral joint and subscapularis muscle. The axillary nerve innervates the deltoid muscle. The main portion of the posterior cord becomes the radial nerve, which travels posterior to the sheath and exits the axillary space along with the axillary sheath. The medial and lateral cords give rise to the median nerve, which is found on the lateral aspect of the sheath and exits the inferior aspect of the axillary space along the sheath. The ulnar nerve arises from the medial cord and travels along the most medial aspect of the sheath. Because of its medial position along the sheath, the ulnar nerve is the most common nerve to be involved by tumors arising inferior to the brachial plexus. This nerve often displays the first symptoms of brachial plexus involvement, which may be either weakness or neuropathic pain.

Axillary Artery and Brachial Artery

The axillary artery is a continuation of the subclavian artery as it passes below the clavicle and over the first rib. As it exits the axillary space just distal to the take-off of the circumflex vessels it is termed the "brachial" artery. This transition occurs at the level of the inferior

pectoralis major and teres major muscles. From an anatomic perspective the axillary artery is considered to consist of three segments. The first segment is the length between the clavicle and pectoralis minor. The second is the area under the pectoralis minor, and the third is the segment between the inferior lateral pectoralis minor border to the point of exit below the teres major muscle. Tumor involvement may occur in any of these three locations. The most common sites for axillary sarcomas are the second and third segments. Metastatic carcinomas involving the axillary space can involve any of these areas; however, they most often present as large, matted tumor masses between areas two and three.

Staging Studies

Three-dimensional imaging of the axillary space is important for accurate anatomical tumor localization and surgical planning (Figures 33.21–33.23). Computed tomography (CT), magnetic resonance imaging (MRI), angiography, and three-phase bone scans are used in the same manner as they are in other anatomic sites. In addition, we have found that venography of the axillary and brachial veins is essential to the evaluation of tumors of the axilla and brachial plexus.

Computed Tomography

CT is most useful in evaluating the bony walls of the axilla, specifically the humerus, glenohumeral joint, and scapula (Figure 33.23). Soft-tissue tumors are well defined by CT scans. CT scans with IV contrast aid in the definition of the axillary vessels.

Magnetic Resonance Imaging

MRI is extremely useful in determining the extent of a soft-tissue mass in the axillary space and the involvement of the underlying serratus anterior and/or the anterior and posterior walls of the axillary space (pectoralis major, subscapularis, latissimus dorsi, and teres major muscles) (Figure 33.21).

Angiography

Angiography should be part of the evaluation of all tumors of the axillary space (Figure 33.21C). It will demonstrate any vascular displacement (very often inferior or anterior) and vascular anomalies of the axillary vessels. In addition, it is useful for evaluating the response to induction chemotherapy; a good response is indicated by a dramatic reduction in tumor vascularity.

Venography

Venography is one of the most accurate means of determining brachial plexus and axillary sheath involvement or infiltration by tumor (see Figure 33.22C). It is routinely performed to evaluate the axillary vein. The arterial wall is thick and rarely shows signs of occlusion, whereas the axillary vein is a thin-walled structure that is easily compressed and infiltrated by tumor. Therefore, occlusion is almost synonymous with vascular sheath and brachial plexus involvement. We have found that a positive venogram showing occlusion of the vein, in combination with neurological pain and weakness, is almost always pathognomonic of axillary sheath and brachial plexus involvement by tumor. The triad of axillary venous occlusion, distal motor weakness, and neuropathic pain is a very reliable predictor of tumor infiltration of the brachial plexus sheath.

Biopsy

Biopsy of axillary tumors should be performed utilizing a core needle or fine-needle aspiration (FNA) technique. If a metastatic lesion is likely, FNA is the most appropriate means to identify carcinoma cells. If one suspects a sarcoma, a core needle biopsy should be performed. The biopsy should be performed through the base of the axillary space, and not through the pectoralis major muscle or near the vascular sheath. This can easily be performed under CT guidance. Deep-seated lesions near the chest wall can also be approached in this manner. Anteromedial lesions, on occasion, can be approached through the lower portion of the pectoralis major muscle. The biopsy site must be removed in its entirety during resection of the tumor.

Surgical Guidelines

1. *Incision.* Anterior utilitarian incision with axillary extension is utilized. This incision extends along the deltopectoral interval then curves inferiorly and distally over the base of the axilla.
2. *Detachment of the pectoralis major muscle.* The pectoralis major is detached from its insertion on the humerus and is reflected towards the chest wall while maintaining its vascular pedicles. This

permits exposure of the entire axillary space and fascial sheaths.

3. *Development of the anterior axillary fascial plane (clavipectoral fascia).* This is a thick, well-defined layer of fascia that contains the entire axillary space and structures. This plane must be developed prior to any further dissection.
4. *Release of the pectoralis minor and conjoined tendon.* The pectoralis minor and conjoined tendon form the anterior muscle layer within the axillary space. Release of these muscles is key to exposure of the vascular sheath, the brachial plexus, and the numerous vascular branches feeding any large tumors.
5. *Identification of the musculocutaneous nerve, radial nerve, and the axillary nerve.* The musculocutaneous nerve comes around the lower border of the coracoid under the pectoralis minor muscle. The axillary nerve comes off deeper from the posterior cord and travels toward the shoulder joint. Both must be identified at this stage.
6. *Mobilization of the axillary sheath and brachial plexus.* Proximal and distal control of the vascular sheath is obtained prior to tumor dissection. Once the deep fascia is opened, and the pectoralis minor muscle is released, the sheath is found very easily by palpation of the axillary fat. Vessel loops are placed around the entire sheath; there is no need to dissect the individual components.
7. *Resection of tumor.* All of the feeding branches entering into the mass are serially ligated and transected. Axillary fat is left around the tumor mass as the only true margin.
8. *Closure.* The pectoralis minor and conjoined tendon are reattached to the coracoid process.
9. *Insertion of catheter.* An epineural catheter is placed in the axillary sheath for postoperative pain relief.
10. *Closure of the empty space.* Following resection, there is often a large empty space that is prone to collect fluid. This may lead to wound complications and dehiscence. To close this space the latissimus dorsi may be released from its insertion onto the humerus, inserted into the defect, and sutured to the subscapularis muscle.
11. *Postoperative management.* The arm is suspended and kept adducted at the side of the body to close off this space. Multiple drains are utilized for 4–7 days.

Surgical Technique

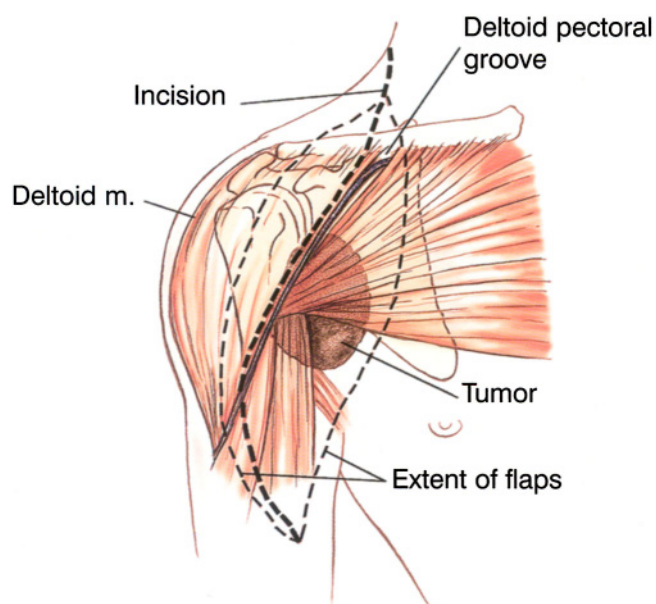


Figure 33.24 Incision. The tumor is shown under the pectoralis major muscle within the axillary space. The patient is placed in a supine semilateral position. The arm, shoulder girdle, and chest are prepared and draped. A deltopectoral incision is used; it starts over the junction of the inner and middle thirds of the clavicle, continues along the deltopectoral groove, and curves distally over the anterior axillary fold (inferior border of the pectoralis major muscle). The superficial fascia is opened, the cephalic vein is ligated or preserved, and medial and lateral fasciocutaneous flaps are raised.

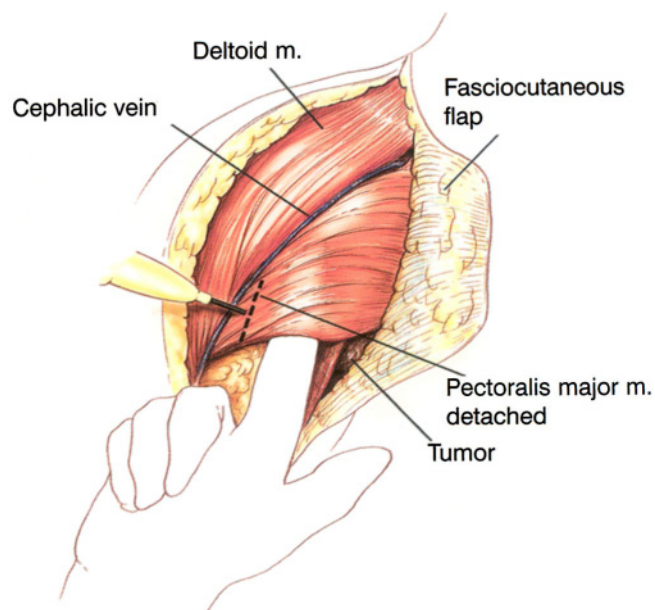


Figure 33.25 Detachment of the pectoralis major. The pectoralis major muscle is detached from its insertion to the proximal humerus, leaving at least 1 cm of the tendon for reattachment. Care must be taken to protect the axillary vessels. Large axillary tumors may displace the axillary sheath anteriorly and adjacent to the pectoralis major muscle.

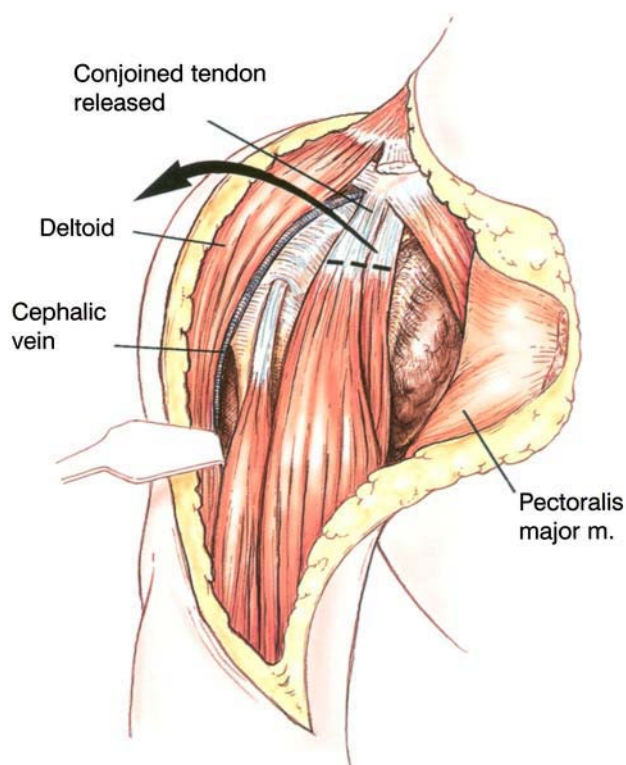


Figure 33.26 (right) Muscle division. The short head of the biceps and coracobrachialis (conjoined tendon) and pectoralis minor muscles are divided at their insertion on the coracoid process. Reflection should be performed with caution to prevent traction injury to the musculocutaneous nerve.

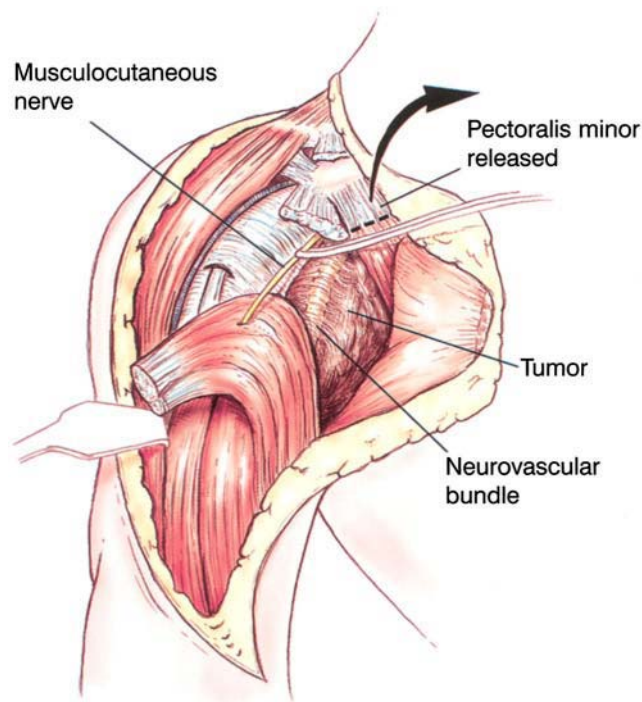


Figure 33.27 Detachment of the pectoralis minor and conjoint tendon. The axillary cavity is exposed after detachment and reflection of two muscle layers. The pectoralis minor muscle is reflected medially, and the conjoint tendon (coracobrachialis and biceps muscles) is reflected caudally. All edges of reflected muscles are tagged with a suture for later identification and use in reconstruction.

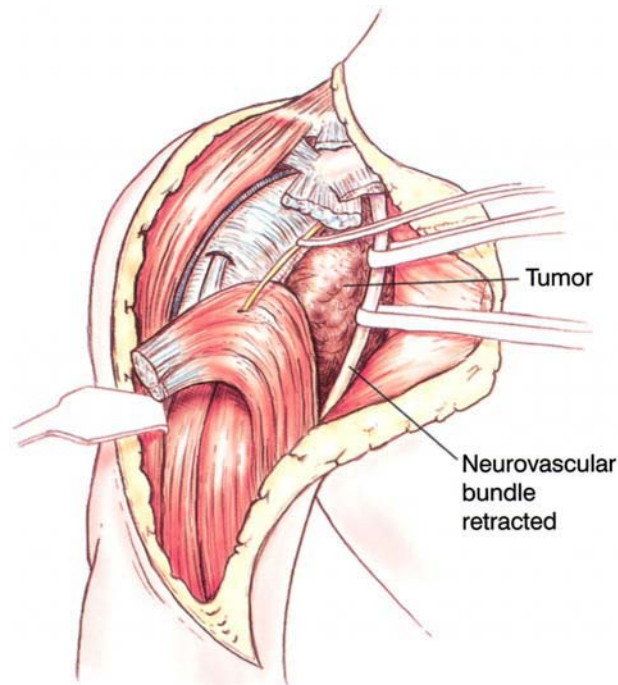


Figure 33.28 The deep axillary fascia, neurovascular bundle, and contents of the axillary cavity are now fully exposed. The anatomic relation of the tumor to the neurovascular bundle can be determined and the decision regarding tumor resectability made. At this anatomic site the artery, vein, and brachial plexus are in close relation, and tumor extension to the neurovascular bundle usually affects all its components and negates resection. Benign tumors and soft-tissue sarcomas usually push the adjacent neurovascular bundle; only at a later stage do soft-tissue sarcomas actually break into it. Metastatic carcinomas directly invade the surrounding tissues, irrespective of compartmental borders. For these reasons, resection of large metastases with preservation of the neurovascular bundle is occasionally not feasible. If the neurovascular bundle is free of tumor, resection of the tumor can proceed. Multiple vascular pedicles must be ligated.

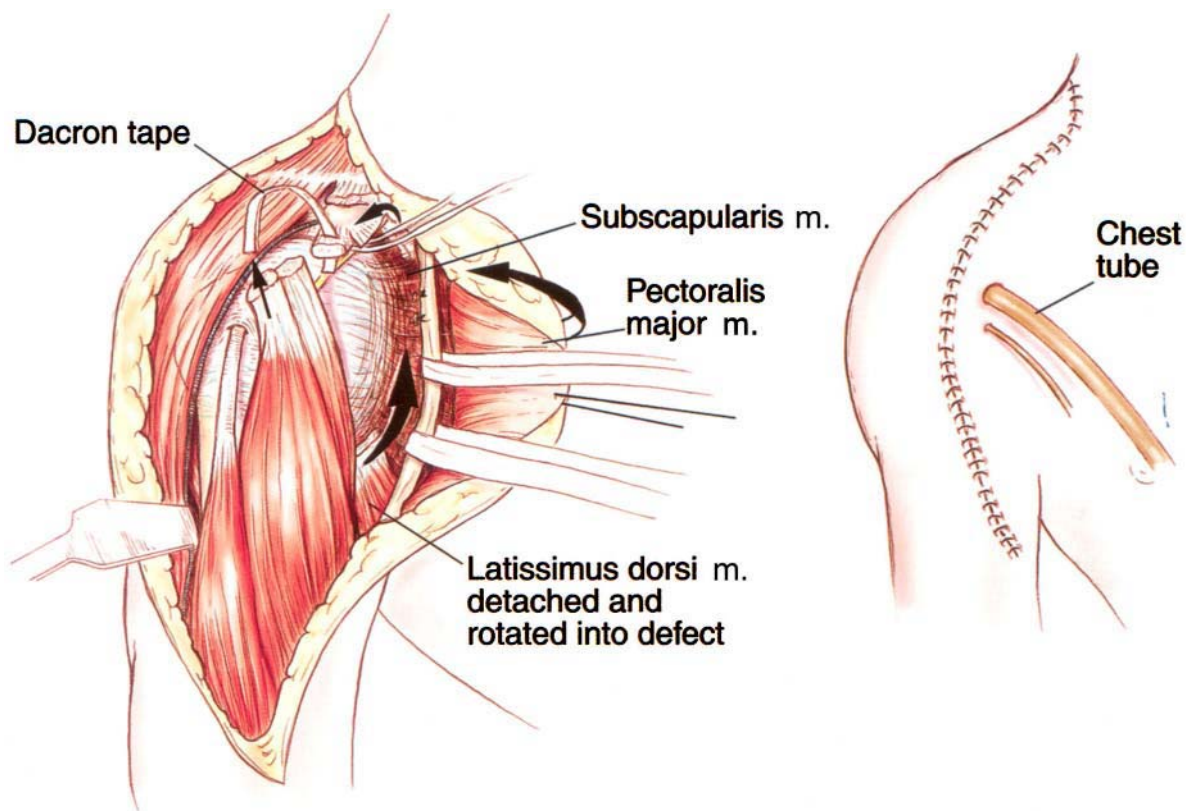


Figure 33.29 Reconstruction of defect and reattachment of the conjoint tendon and pectoralis minor muscles and closure. Following resection the pectoralis minor and conjoint tendons are reattached to the coracoid process with a nonabsorbable suture, and the pectoralis major is reattached to its insertion site on the proximal humerus in the same manner. The wound is closed over suction drains. The upper extremity is placed in an arm sling. Continuous suction is required for 4–7 days; perioperative intravenous antibiotics are continued until the drainage tubes are removed. Postoperative mobilization with gradual range of motion of the shoulder joint is then introduced.

Figure 33.30 (see following page) Anterior axillary mass arising from the scapula. (A) Clinical photographs shows a large axillary tumor (T) underlying the pectoralis major muscle and arising from the anterior surface of the scapula and subscapularis muscle. This tumor was easily palpable immediately below the pectoralis major muscle. Surgical exposure (B–D): a transpectoralis axillary incision was utilized to expose the axillary space and brachial plexus and vessels prior to resection of the scapula from the posterior approach. The combination of the anterior and posterior approaches is termed the "utilitarian" surgical approach for the shoulder girdle. (B) Intraoperative photograph shows the pectoralis major muscle (solid arrow) that makes up the anterior wall of the axilla. This muscle is detached through the deltopectoral interval from the insertion onto the humerus and is reflected towards the chest wall, exposing the axillary contents and the pectoralis minor (large solid arrow) muscles are exposed and released from the coracoid. (C) Deep layer of muscle (small arrow), the coracobrachialis, and the short head of the biceps inserts onto the coracoid. The entire axillary space is now easily visualized. The clavi-pectoral fascia, encloses the entire space (small arrow). (D) Surgical dissection of the infraclavicular portion of the brachial plexus (Penrose drain and vessel loop) demonstrating a large anterior mass (T, solid arrow) that displaces the sheath anteriorly. Note the intimate apposition of the vascular sheath to the tumor (small arrows). This approach is an extremely safe and reliable method of mobilizing the brachial plexus in patients with large tumors of the axillary space.

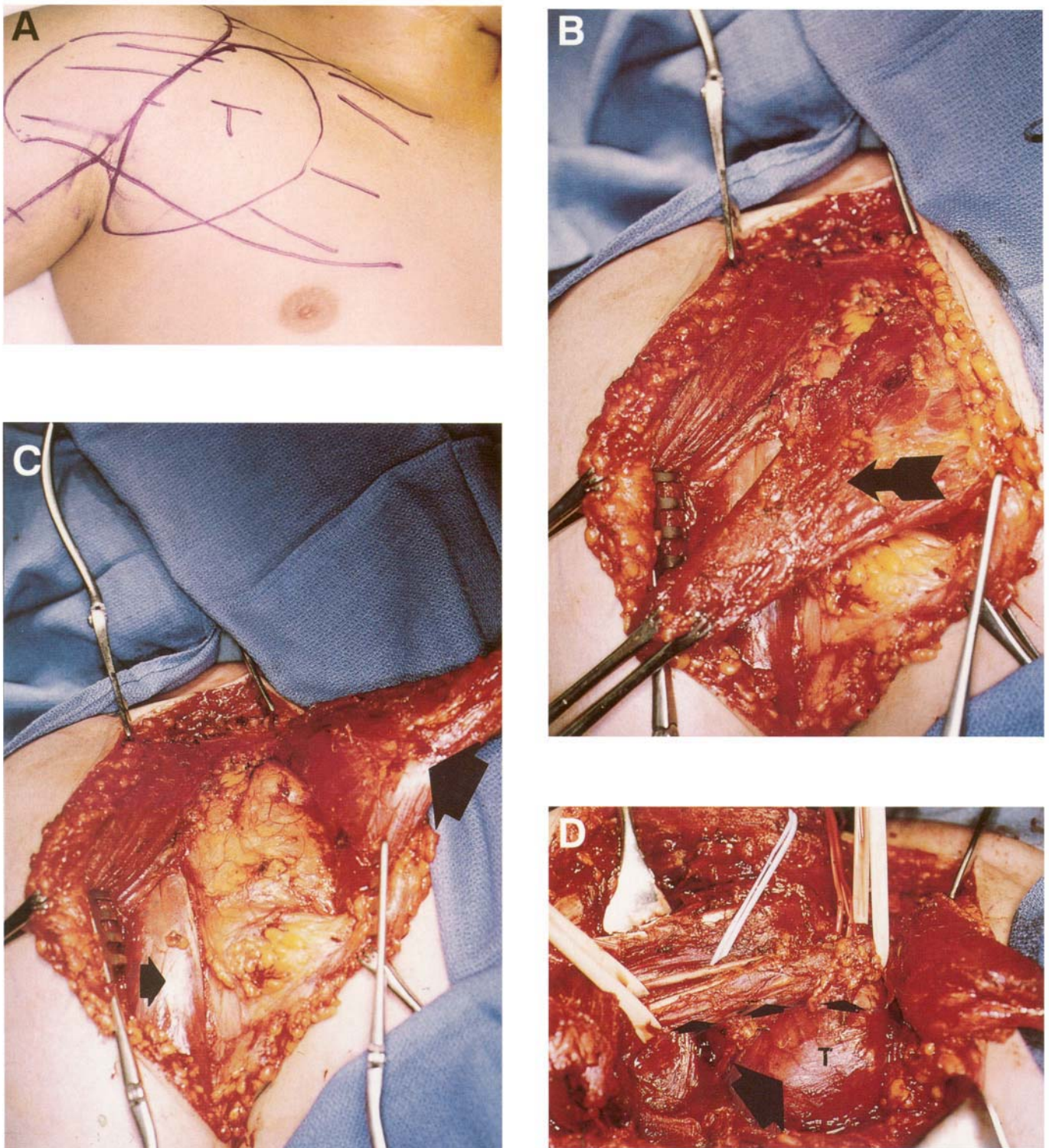


Figure 33.30 A-D

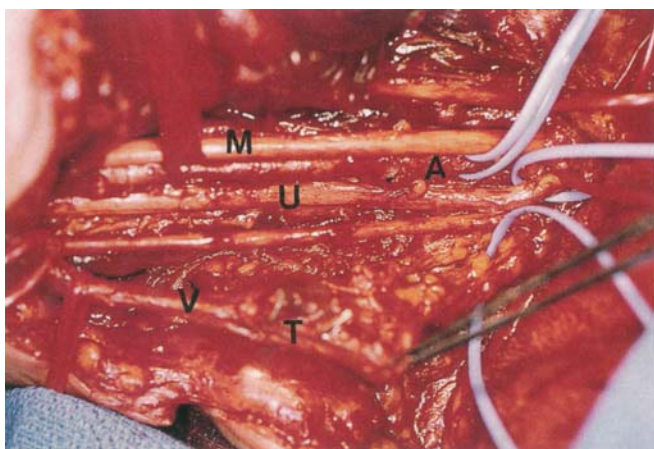


Figure 33.31 Infraclavicular plexus dissection for hemangioendothelioma of the axillary vein presenting with ulnar nerve symptoms. This is an intraoperative photograph of the infraclavicular portion of the brachial plexus in which the sheath had been completely opened and all five terminal nerves identified. The terminal five nerves of the brachial plexus are: musculocutaneous, axillary, radial, ulnar, and median. The transpectoralis approach was utilized for this resection. This patient has been initially treated by inadequate resection through a small axillary incision that necessitated this re-exploration and resection. The axillary vein has been retracted and the axillary artery is identified. The tumor (T) arose from the wall of the axillary vein and was pressing on the medial cord and ulnar nerve, accounting for the ulnar nerve symptoms.

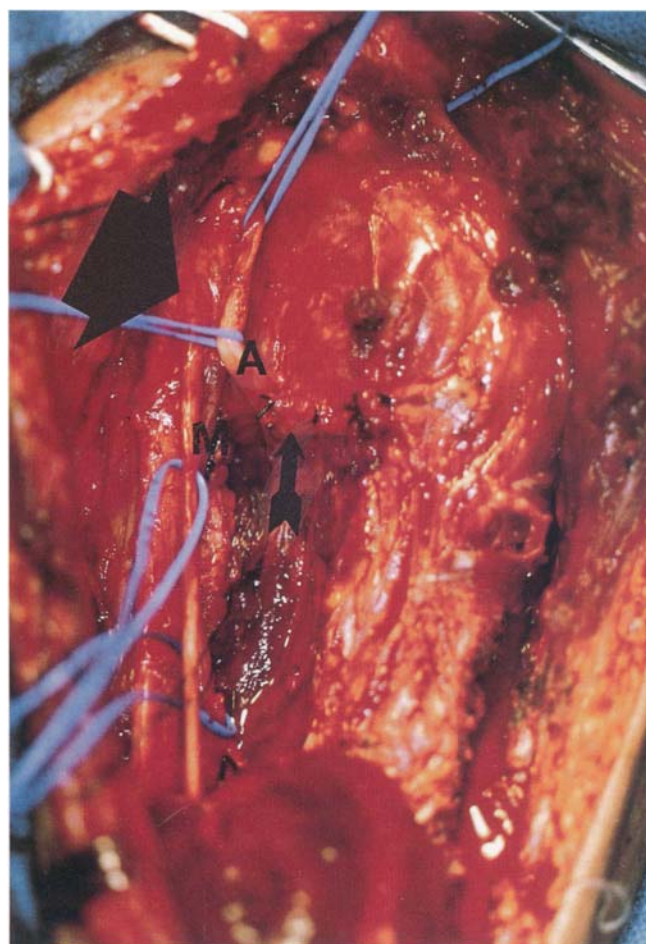


Figure 33.32 Intraoperative photograph following an intra-articular resection of a proximal humerus osteosarcoma. The pectoralis major muscle had been detached from the humerus and reflected toward the chest wall. The deeper layer, consisting of the conjoint tendon and pectoralis minor muscles, was detached from the coracoid and reflected medially. This exposes the infraclavicular plexus (large solid arrow). The musculocutaneous (M) and axillary nerves (A, superior vessel loop and small arrow) were initially dissected and preserved. Intra-articular resections require preservation of the axillary nerve (A). This approach is extremely useful for large tumors of the proximal humerus with an extrasosseous component.

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Scapulectomy

Martin Malawer, James Wittig and Cynthia Rubert

OVERVIEW

The scapula is a relatively common site for primary bone tumors, including chondrosarcoma and renal-cell carcinoma in adults and Ewing's sarcoma in children. Soft-tissue sarcomas may arise from the suprascapularis or other rotator cuff muscles and may secondarily invade the scapula. Tumors arising from the scapula are often initially contained by muscle, thereby protecting other tissues. Important anatomic areas to evaluate for tumor extension are the chest wall, axillary vessels, brachial plexus, proximal humerus, glenohumeral joint, and rotator cuff.

Shoulder motion and strength are nearly normal following a partial scapular resection (Type II). However, there is significant loss of shoulder motion, predominantly shoulder abduction, following a total scapular resection (Type III), alone or in conjunction with an extra-articular resection of the shoulder joint and proximal humerus (Types IV and VI). Suspension of the proximal humerus and meticulous soft-tissue reconstruction are the keys to providing shoulder stability and a functional extremity. If significant periscapular muscles remain following tumor resection (especially the trapezius and deltoid muscles), a total shoulder–scapula prosthesis may be the optimal reconstructive option.

This chapter discusses the anatomic and surgical considerations of limb-sparing scapular resections and describes the techniques of resection and reconstruction. Additional information regarding the indications and contraindications of limb-sparing resection, surgical staging and classification, endoprosthetic reconstruction and design features, and functional and rehabilitation considerations may be found in Chapter 9.

INTRODUCTION

Tumors arising from the scapula may become quite large before they are diagnosed (Figure 34.1). Initially, they are often contained by muscle, thereby protecting other tissues. They often present with pain, a mass, or both. Chondrosarcomas are the most common primary malignancy of the scapula in adults; in children the most common primary malignancy of the scapula is Ewing's sarcoma (Figure 34.2). Soft-tissue tumors may involve the periscapular musculature and secondarily invade the scapula.

The first limb-sparing attempts involved tumors of the scapula. The first description of a scapular resection was published by Liston in 1820 and involved an ossified aneurysmal tumor.¹ Syme² performed a near-total scapulectomy with resection of the clavicle in 1856. In 1909 De Nancrede³ concluded that all shoulder girdle tumors should be treated with a forequarter amputation. Since De Nancrede's paper, several authors have described modifications of scapular resections and different indications.

Today, the majority of malignancies of the shoulder girdle can be treated safely with limb-sparing surgeries. Indications for limb-sparing surgeries at this location include most high-grade bone sarcomas and some soft-tissue sarcomas, depending on the tumor extent. Scapular tumors, like tumors of the proximal humerus, require careful preoperative staging, appropriate imaging studies, and a thorough knowledge of local anatomy. Selection of patients whose tumor does not involve the neurovascular bundle, thoracic outlet, or adjacent chest wall is required. Forequarter amputation is indicated mainly for patients with large, fungating tumors, or infected tumors; those in whom limb-sparing resection has failed; and those with tumors invading the major nerves and vessels or chest wall.

A classification system for resection of tumors of the scapula and shoulder girdle is described in Chapter 9. The most common resection for a high-grade tumor of the scapula, a Type IV-B (true Tikhoff–Linberg), is illustrated in this chapter (Figure 34.3).

As with other types of shoulder girdle resections, optimal function is achieved by local muscle transfers and skeletal reconstruction. A total scapular prosthesis may be used if adequate soft tissues remain. A stable shoulder girdle that allows positioning of the elbow and hand for functional activities is the goal of shoulder girdle reconstruction.

UNIQUE ANATOMIC CONSIDERATIONS

A limb-sparing procedure involving the shoulder girdle is more difficult than a forequarter amputation. The

surgical options are technically demanding and fraught with potential complications. The local anatomy of the tumor often determines the extent of the required operation. One should be experienced with all aspects of shoulder girdle anatomy and the unique considerations presented, which are as follows.

Scapula

Tumors of the scapula often become quite large before being brought to a physician's attention. In the early stages of development they are surrounded by a cuff of muscle in all dimensions (infraspinatus, subscapularis, and supraspinatus). Important areas to evaluate are the chest wall, axillary vessels, proximal humerus and rotator cuff, and pericapsular tissue.

Glenohumeral Joint

Sarcomas involving the glenoid, scapular neck, or supraspinatus area usually involve the joint and adjacent capsule. Therefore, an extra-articular resection through a combined anterior and posterior approach (see Surgical Techniques section) should be performed for tumors in this location.

Neurovascular Involvement

As sarcomas of the scapula enlarge, they may produce a large axillary and/or anterior component and involve the axillary vessels and brachial plexus. When there is a large anterior extraosseous mass, anterior exploration of the neurovascular bundle should be performed to determine resectability or facilitate an extra-articular resection safely.



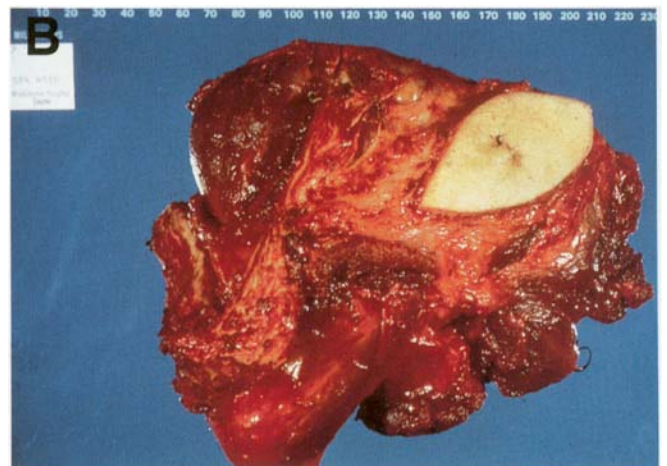
Figure 34.1 CT scan of an extremely large scapular tumor with extension to the chest wall and involvement of all of the adjacent muscles.



Figure 34.2 (A) Typical chondrosarcoma of the scapula with a large extraosseous component showing soft-tissue calcifications. Chondrosarcoma is the most common primary bone tumor of the scapula. It usually occurs past the third decade of life. (B) Ewing's sarcoma of the scapula. Ewing's sarcoma usually occurs in patients less than 20 years of age. This patient had undergone a partial resection (hemoclips) with recurrence that required a total scapular resection and proximal humeral resection (Type IV, Tikhoff-Linberg Resection). (C) Total scapula prosthesis. This is the original design utilized in the late 1980s. Note that there are only a few holes for muscle attachments and the scapula body is solid. Gore-Tex graft is sutured around the glenoid and proximal humerus recreating a joint capsule.



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Figure 34.3 (A) Plain radiograph following a classical Tikhoff-Linberg resection of the scapula. This is now classified as a Type IV resection. (B) Gross specimen showing the scapula and overlying muscles with the biopsy site en-bloc. (C) Clinical photograph 16 years following the photograph shown above, demonstrating a one-handed push-up. This illustrates the excellent shoulder girdle stability following reconstruction without a scapular prosthesis if there are significant muscles available to be transferred to the clavicle and the humerus. (D) The same patient rowing a boat. The clinical appearance of the shoulder is facing the reader.

Lymph Nodes

The axillary and supraclavicular lymph nodes should be carefully examined preoperatively. Lymph node biopsy may be necessary to determine resectability.

Suprascapular Tumors

This is a difficult area to evaluate by physical exam and even with modern imaging techniques. Large tumors in this location often extend into the anterior and posterior triangles of the neck, making resection difficult or contraindicated, except for purposes of palliation.

INDICATIONS

A limb-sparing resection is indicated for most low- and high-grade sarcomas of the scapular and periscapular soft-tissues that secondarily invade bone. Contra-indications include tumor extension into the axilla with involvement of the neurovascular bundle, and extensive involvement of the adjacent chest wall. Complications from a prior biopsy with extensive contamination of tissues may also make a limb-sparing scapular resection inadvisable.

IMAGING STUDIES

Necessary preoperative imaging studies include plain radiographs, computed tomography (CT) scan, magnetic resonance imaging (MRI), bone scan, arteriography, and occasionally venography. These studies are crucial for evaluation of tumor extension into the chest wall, axillary vessels, proximal humerus and glenohumeral joint.

CT and MRI are the most valuable means of determining the size and extent of extraosseous disease and its relationship to the axillary vessels, glenohumeral joint and chest wall.

Arteriography can determine vascular involvement as well as vascular anatomy. Displacement of the axillary vessels is indicative of anterior tumor extension into the axilla. This mandates an anterior approach to permit safe mobilization of the axillary vessels and the brachial plexus. Axillary venography is performed if there is any clinical suspicion of brachial plexus involvement. Nerve pain and/or distal edema is the hallmark of invasion and not just displacement of the brachial plexus. Occlusion of the axillary vein as seen on venography correlates with brachial plexus infiltration and is indicative that an amputation may be required. Bone scan may indicate rib involvement and is useful for evaluating proximal humeral extension and metastatic disease.

BIOPSY

The biopsy site should be carefully selected. It should be located away from the major vessels and nerves and placed so that it can be widely excised by the definitive resection. Inadvertent contamination of the neurovascular structures or the chest wall must be avoided. Sarcomas of the shoulder girdle rarely require an open biopsy. The majority of sarcomas in this location have an extraosseous (soft-tissue) component; therefore a small-needle or core biopsy should be performed.

Fine-needle or core biopsies should be performed under fluoroscopic or CT guidance unless the mass is easily palpable and located away from the neurovascular bundle. Only one puncture site is required. The needle is then reintroduced through the same puncture site, but the angle is varied so cores can be obtained from several different regions of the tumor. Touch-preps and frozen sections are performed at the time of biopsy to confirm that adequate tissue has been obtained. Cultures are routinely obtained irrespective of the suspected diagnosis because infection may simulate any malignancy.

Scapula

Biopsies of the scapular body are more difficult to perform than biopsies in other sites; however they are crucial for determining the final operative procedure. The biopsy site should be along the intended incision site of the resection. A posterior needle biopsy is recommended for tumors arising within the body of the scapula; the anterior approach should be avoided. Biopsies of tumors of the scapula should be performed along the lateral or axillary aspect of the scapula. The biopsy should not be along the vertebral (medial) border or directly posterior through the potential skin flap.

SURGICAL GUIDELINES

1. A combined anterior and posterior approach is utilized (utilitarian shoulder girdle incision).
2. The axillary vessels and plexus are explored and mobilized anteriorly. This requires the pectoralis major to be detached and reflected for adequate exposure.
3. The posterior incision permits the release of all muscles attaching to the scapula.
4. The glenohumeral joint is removed extra-articularly. The osteotomy is performed below the level of the joint capsule.
5. The remaining humerus is supported from the clavicle with Dacron tape (static suspension) and the conjoint tendon (dynamic suspension).

6. A scapular prosthesis may be utilized if significant musculature remains; specifically the deltoid, trapezius, rhomboids, serratus anterior, and latissimus dorsi muscles are required for a prosthetic replacement.
7. Postoperatively, a sling is required for 4–6 weeks.

SURGICAL TECHNIQUE

Extra-articular Total Scapula and Humeral head Resection (Type IV); the Tikhoff–Linberg Procedure (Figure 34.3)

This procedure is indicated for most high-grade sarcomas of the scapula, especially if tumor extends anteriorly or laterally and involves the rotator cuff, glenoid, or glenohumeral joint. It is also used for some low-grade sarcomas of the scapula and for periscapular soft-tissue sarcomas. In general, a total scapulectomy (intra-articular; Type III) resection is a poor cancer operation since it does not remove all tissue at risk of involvement from origin to insertion.

The resection consists of en-bloc removal of the scapula, distal clavicle, and proximal humerus with preservation of the arm. It includes removal of all the muscles arising from the scapula and inserting on the proximal humerus and an extra-articular resection of the glenohumeral joint. The interval between the tumor and neurovascular bundle must be carefully evaluated; this requires surgical exploration prior to resection. Occasionally, the deltoid muscle and the axillary nerve can be preserved. In this situation a total scapula prosthesis may be used for reconstruction.

Reconstruction

Soft-tissue reconstruction is necessary to provide stability and avoid a flail upper extremity. The extent of proximal humeral resection and the muscles remaining available for reconstruction and coverage dictate the type of reconstruction performed. The preferred techniques include a standard dual suspension (i.e. static and dynamic) technique using Dacron tape and the remaining bone and muscle for reconstruction or, if adequate soft tissue is preserved, total scapula and proximal humerus prostheses (Figures 34.2 and 34.3).

Standard Reconstruction (Dual Suspension)

The dual suspension technique is performed. Dacron tape (3 mm) is used to suspend the remaining humerus from the distal clavicle. The biceps, coracobrachialis and triceps are reattached through drill holes in the distal clavicle. If the deltoid muscle has been preserved, it is tenodesed anteriorly to the pectoralis major and

trapezius muscles to further reconstruct the anterior musculature of the shoulder girdle.

SCAPULAR PROSTHETIC RECONSTRUCTION

Experience with total scapular replacement is limited but increasing (Figure 34.4). We have performed 25 scapular prosthetic replacements. Three issues need to be addressed for successful prosthetic reconstruction following a Type IV resection:

1. replacing the proximal humerus;
2. creating a new glenohumeral joint;
3. providing soft-tissue attachments to both the humeral and scapular components to improve stability and function.

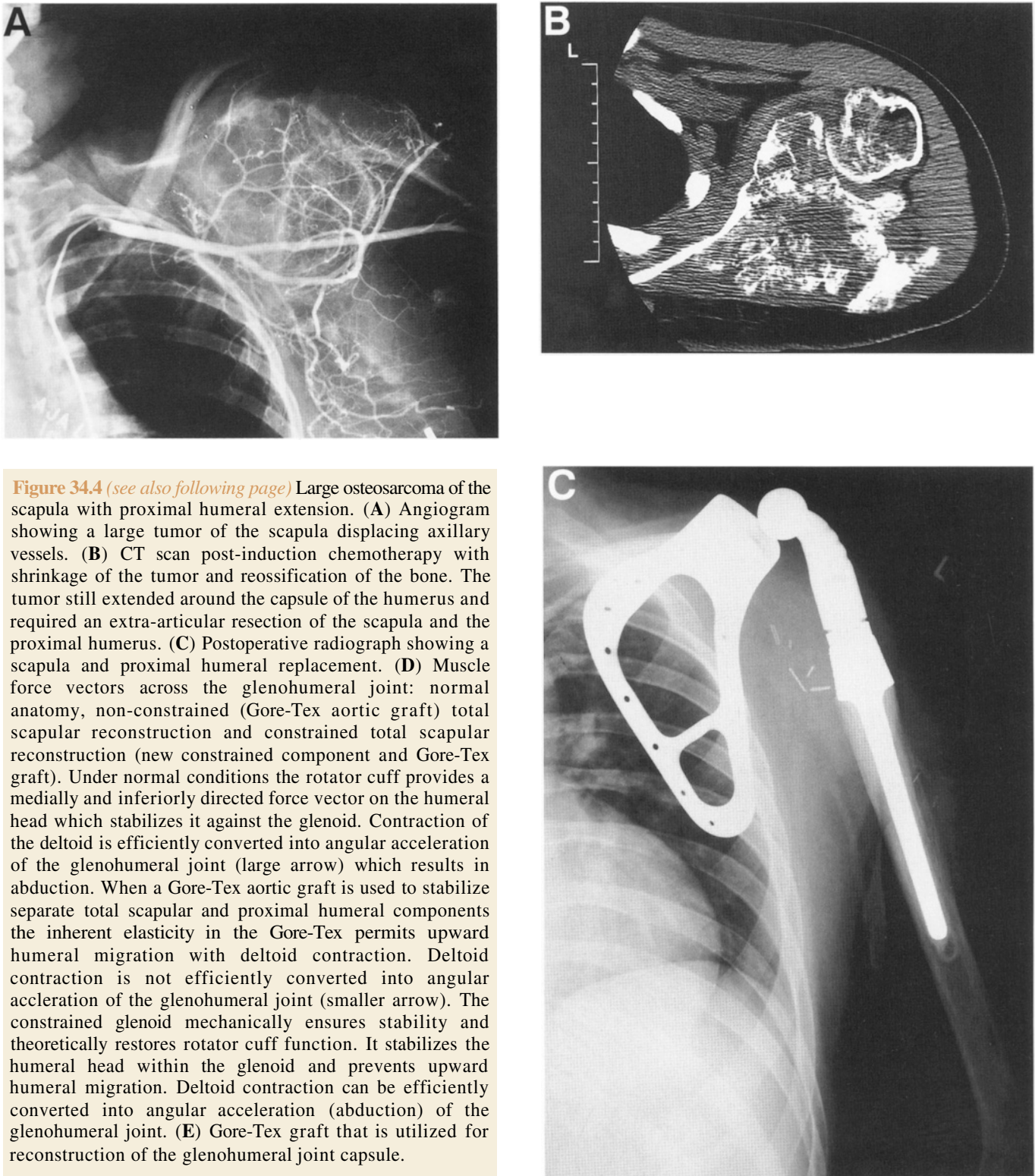
A total scapular and glenohumeral joint prosthesis is used for reconstruction following a Type IV resection. It is imperative that adequate muscle be preserved for complete coverage of the prosthesis following soft-tissue reconstruction. This requires the deltoid, trapezius, rhomboids, serratus anterior, and latissimus dorsi muscles. If limited muscle remains following tumor resection, the standard dual suspension reconstruction should be performed.

Several prosthetic devices are available for reconstruction of the glenohumeral joint. Most are constrained or semiconstrained devices; i.e. they provide shoulder stability. The body of the prosthetic scapular design has large fenestrations that decrease its weight and allow tenodesis of the overlying muscle to the underlying serratus anterior muscle and chest wall. Multiple holes along the axillary, glenoid, and vertebral borders of the scapular component, as well as holes or loops along the proximal humeral component, are available for soft-tissue reattachments.

The proximal humeral prosthetic component or the humeral resurfacing component (if minimal bone resection is required) is cemented into the remaining humeral diaphysis using the techniques previously described.

CONSTRAINED TOTAL SCAPULAR PROSTHESIS (Figure 34.4D)

The rotator cuff muscles actively stabilize the glenohumeral joint during active shoulder abduction and forward flexion. Their function is coupled with the deltoid and trapezius muscles to produce 180° of motion. During glenohumeral abduction, deltoid contraction produces an upward force vector on the proximal humeral shaft while the rotator cuff produces an inward and downward force on the humeral head. The rotator cuff prevents upward humeral migration



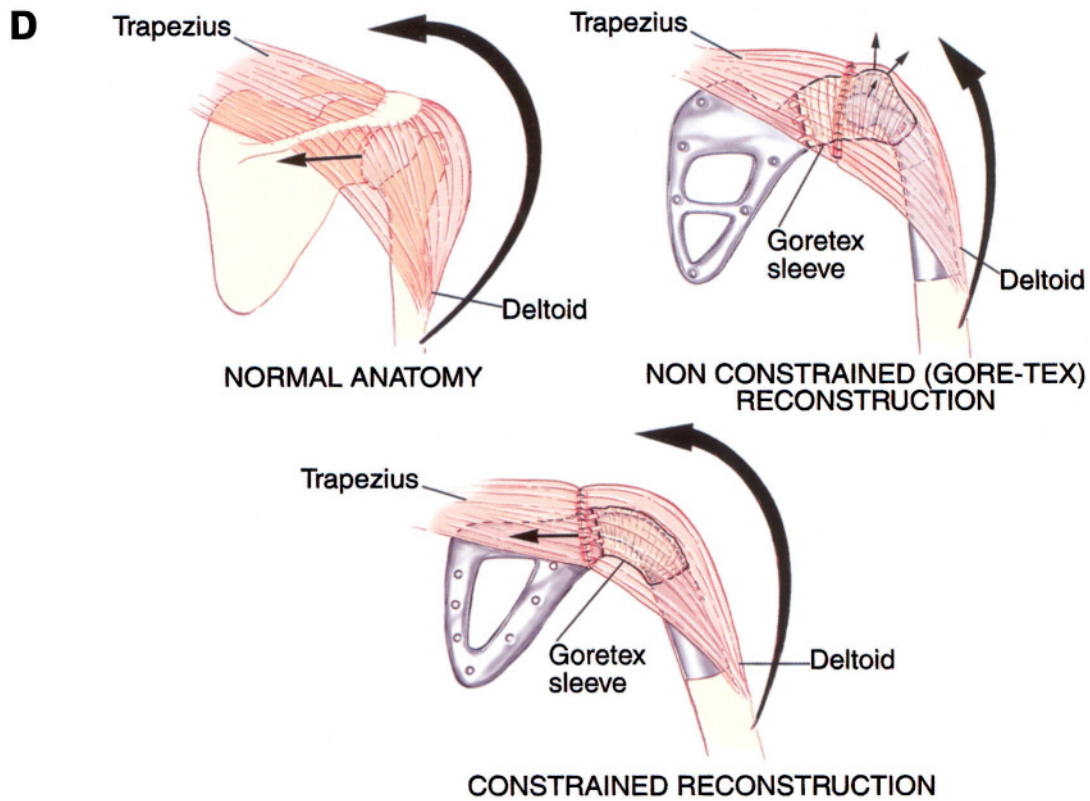
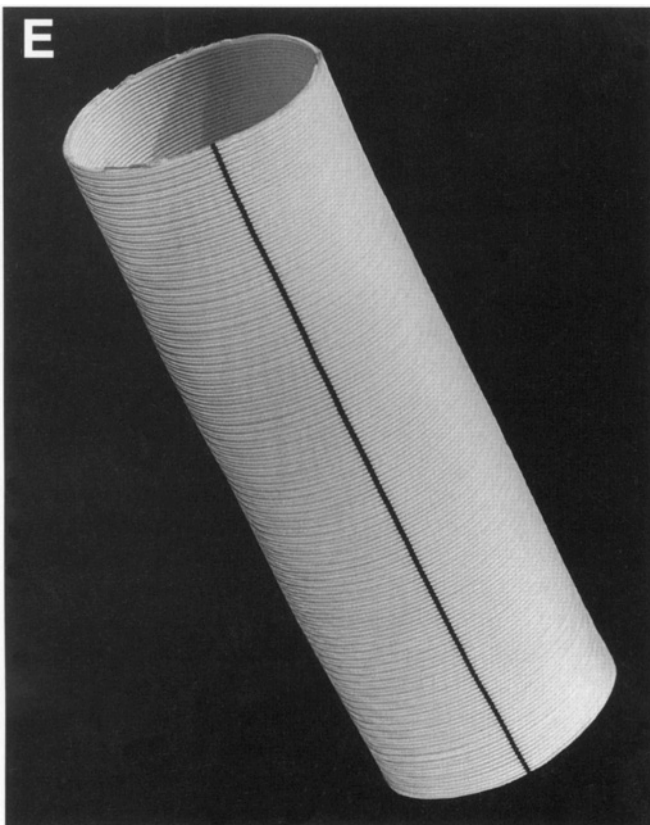


Figure 34.4 D,E



by stabilizing the humeral head in the glenoid fossa, thus creating a fixed fulcrum at the glenohumeral joint. The upward force produced by the deltoid is converted into angular acceleration at the glenohumeral joint, which facilitates shoulder abduction/elevation. Without the rotator cuff the humerus translates superiorly with deltoid contraction. The forces produced by the deltoid are dissipated and fail to result in angular acceleration.

The major advantage of the constrained (scapula) glenohumeral joint in lieu of a nonconstrained scapula is that it increases shoulder stability but, most importantly, passively substitutes for the function of the absent (resected) rotator cuff by creating a fixed fulcrum at the glenohumeral joint. This permits the deltoid to function more efficiently.

High-grade sarcomas arising from the scapula require en-bloc resection with the rotator cuff. Anatomic reconstruction with a total scapular replacement recreates both glenohumeral and scapulothoracic mechanisms which are necessary for optimal shoulder function. Traditionally, separate scapular and proximal

humerus components were utilized and stabilized to each other with a Gore-Tex aortic graft. The inherent elasticity in the aortic graft was not ideal for replacing the function of the rotator cuff and occasionally failed by rupturing. In an effort to improve stability at the glenohumeral joint, and replace the function of the rotator cuff, a constrained total scapular replacement, modeled after a bipolar hip hemiarthroplasty, was designed. The constrained glenoid provides a locking mechanism into which the humeral head is snapped without compromising motion. The locking mechanism passively substitutes for the rotator cuff by securing the humeral head within the glenoid fossa that creates a fixed fulcrum at the glenohumeral joint. Deltoid contraction can be efficiently translated into angular acceleration at the joint and therefore active glenohumeral abduction and elevation. Clinically, our experience has shown approximately a 45–60° abduction gain with the new constrained total scapula.

Glenohumeral Capsule Reconstruction

The glenohumeral joint and capsule are reconstructed using a 32-mm Gore-Tex aortic graft that is sewn over the prosthetic scapular neck, attached with Dacron tape, and sutured through holes of the proximal humeral component using multiple Dacron tapes. This stabilizes the new glenohumeral joint (Figures 34.4E and 34.5A–C).

Muscle Reconstruction

The anterior muscle reconstruction follows the techniques used after Type V resections. The biceps and coracobrachialis are sutured together and reattached to the clavicle. The pectoralis major muscle is closed anteriorly over the new joint. The posterior muscle reattachment and reconstruction are described below.

Posterior Muscle Reconstruction

When performing a dual suspension technique, the levator scapulae is tenodesed to the trapezius muscle and sutured to the posterior deltoid muscle at the level of the previous position of the scapular spine. The rhomboids are sutured to the cut edges of the serratus anterior if adequate length remains; otherwise these muscles are sutured to the chest wall or the superior border of the latissimus dorsi.

If a total scapular prosthesis is used, reconstruction of the muscles over the entire prosthesis is imperative. The scapular prosthesis is laid on the chest wall on top of the remaining serratus anterior muscle. Medially, the rhomboids and levator scapulae muscles are reattached.

The latissimus dorsi muscle is advanced superiorly to cover the body of the prosthesis. The trapezius and the posterior deltoid muscles are then tenodesed to provide complete coverage of the prosthesis.

Skin Closure

Large-bore suction catheters or a 28-gauge chest tube are used for drainage. The flaps are closed using nonabsorbable suture, their undersurface is tacked to the underlying muscle to decrease dead space. The skin is closed using staples or suture. Epineural catheters are routinely used with a continuous marcaine (4–8 ml of 0.25% marcaine) infusion for 3–5 days (Figure 34.5D).

TOTAL SCAPULECTOMY

Type III (Intra-articular Scapular Resection)

Total scapulectomy is primarily indicated for sarcomas (usually low-grade) of the scapular body (below the scapular spine). Preoperative considerations are similar to those of the Tikhoff–Linberg resection. If tumor extends anteriorly, or laterally to involve the glenoid or rotator cuff, this procedure is not recommended. An extra-articular resection (Type IV) should be performed. In general, total scapulectomy (Type III resection) is a poor operation to perform for most sarcomas.

Position and Incision

The patient is placed in a semilateral position with the arm prepared and draped free for intraoperative manipulation. A posterior incision is performed and skin flaps are created in a method similar to that used for the Tikhoff–Linberg (Type IV) resections.

Muscle Release

All muscles are transected away from the bone. This process begins with release of the posterior deltoid from the acromion and scapular spine and continues with release and retraction of the trapezius muscle. The latissimus and rhomboid muscles are released starting at the inferior angle of the scapula. The tip is then elevated and the scapula is retracted away from the chest wall as muscle release continues medially, laterally, and then superiorly. This permits manual exploration of the chest wall and axilla.

Axillary Exposure

The inferior tip of the scapula is rotated, and traction is applied with the arm abducted. This permits access to

and identification of the axillary contents, which are then bluntly retracted away from the operative field.

Neurovascular Bundle

The neurovascular structures are approached from the back, unless the tumor has an anterior extraosseous component. They are visualized as the scapula is retracted cephalad and away from the chest wall. Extreme care should be taken to avoid injuring the axillary nerve near the inferior border of the subscapularis muscle and the musculocutaneous nerve as it exits near the coracoid. An anterior incision is recommended if there is any problem in identifying the neurovascular structures.

Shoulder Joint Inspection and Release

Once the body of the scapula is free, attention is turned to the shoulder joint. The infraspinatus and supraspinatus muscles are transected and the joint is entered. Dissection proceeds only if the joint appears normal and without tumor extension. The anterior capsule and the subscapularis tendon are transected. The long head of the biceps is identified, tagged with suture, and divided.

Anterior Resection and Release

The acromioclavicular joint is entered and released or the distal portion of the clavicle is resected with the specimen. As the scapula is gently elevated, the short head of the biceps and the coracobrachialis and pectoralis minor muscles are released from the coracoid. The musculocutaneous nerve must be protected as it passes near the coracoid.

Reconstruction

The dual suspension technique using Dacron tape to suspend the proximal humerus from the clavicle or a total scapular prosthesis can be employed to reconstruct the defect. A scapular prosthesis should be used only if there is significant muscle remaining to cover the prosthesis and provide stability.

PARTIAL SCAPULECTOMY

Type II Resection (Inferior Scapular Body Resection)

This procedure is indicated for low-grade sarcomas and benign lesions of the scapular body. The most common and only practical partial scapular resection involves the portion inferior to the scapular spine. This resection retains sufficient bone and shoulder girdle musculature so that a formal reconstruction is not necessary. The

most common indications are large sessile osteochondroma and low-grade chondrosarcoma.

Posterior Approach and Resection

The incision and approach is identical to that used for Type III resections. After release of the trapezius muscle the resection begins inferiorly with release of the latissimus dorsi from the inferior angle and subsequent elevation of the tip of the scapula. The rhomboid muscles are released medially, and the teres major and minor laterally. If the infraspinatus muscle can be saved, it is elevated from the scapular surface. An osteotome or saw is used to osteotomize the scapula just distal to the scapular spine. This portion of the scapula is elevated and the underlying subscapularis muscle is preserved or is divided and removed with the specimen, depending on the type of tumor.

Reconstruction

The resected portion of the scapula does not need to be replaced. Reconstruction consists of suturing the remaining muscles to the retained portion of the scapula with Dacron tape and tenodesing the rhomboids, latissimus dorsi, and teres muscles together.

PARTIAL SCAPULECTOMY – GLENOID RESECTION

Glenoid Resection

Small tumors involving the glenoid, but not the shoulder joint, are extremely rare. The glenoid may be resected

Figure 34.5 (see following page) (A) Total scapula prosthesis. Note the holes along the vertebral and axillary border as well as the glenoid for reattachments of the adjacent muscles with Dacron tape. The proximal humerus snap fits into the constrained glenoid. (B,C) Surgical technique of reconstruction of the capsular mechanism of the total scapula and proximal humerus with a Gore-Tex graft. (B) shows the graft sewn in place along the glenoid rim with Dacron tape. (C) The Dacron tape is pulled over the proximal humerus and sutured through the corresponding holes with Dacron tape. This technique re-creates the stability of the glenohumeral joint. (D) Postoperative epineural injection of a brachial plexus catheter utilized for postoperative pain relief. We routinely place catheters in the neural sheath of all patients undergoing resection and amputation about the shoulder girdle prior to closing the wound. This provides excellent pain relief during the perioperative period. Note that the dye (solid arrow) is tracking proximally (curved arrow indicates the epineural catheter in the nerve sheath). This catheter is uneventfully removed on the fourth to fifth postoperative day.

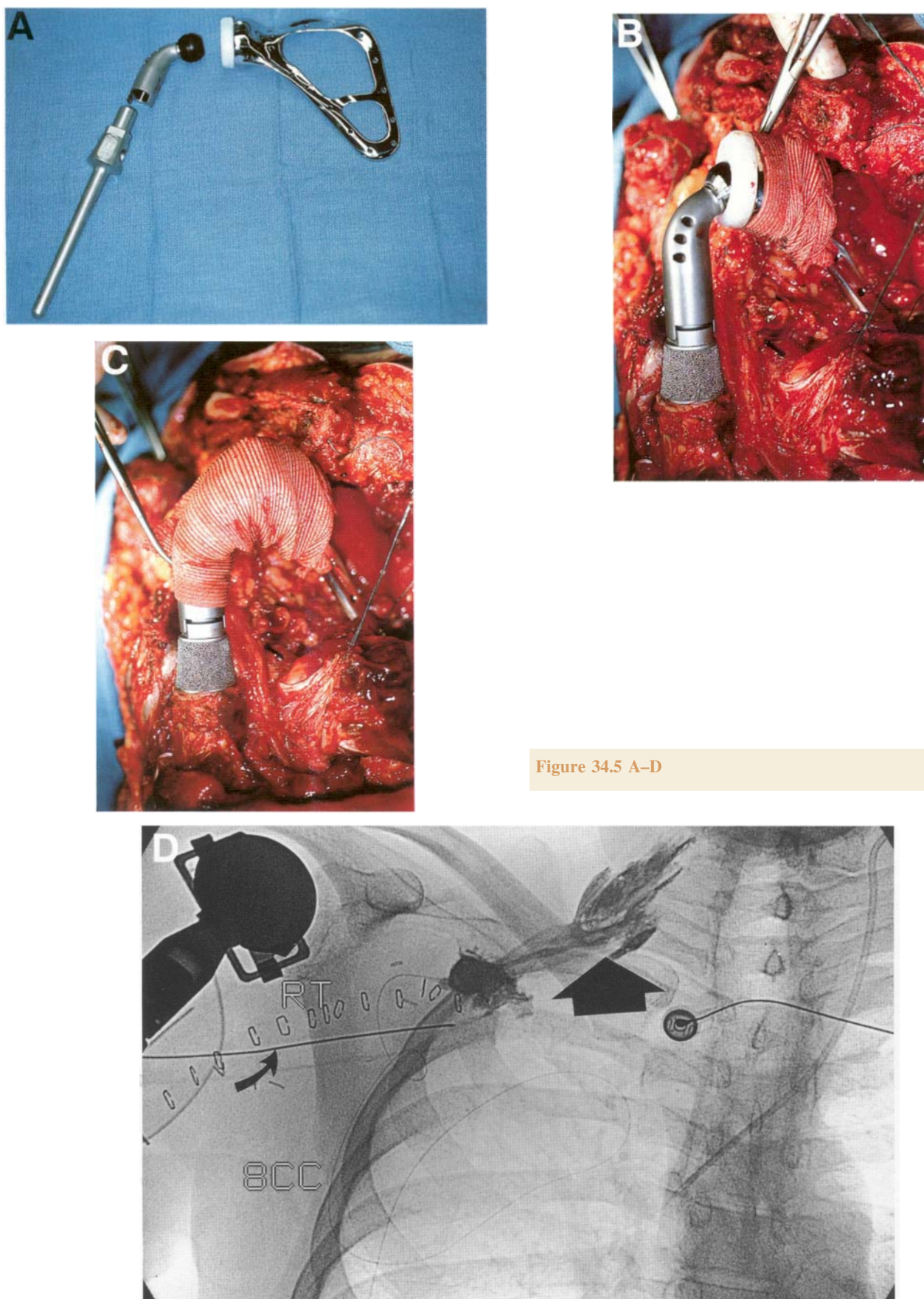


Figure 34.5 A-D

with preservation of the medial scapula. Saving the remaining scapula improves suspension of the upper extremity and offers the possibility of shoulder arthrodesis. This is a rare procedure and is not indicated for bone sarcomas.

Incision and Resection

The resection is done through the anterior approach, with the incision extending from the acromioclavicular joint superiorly, and along the deltopectoral groove to the level of the deltoid insertion. The anterior deltoid is released from the clavicle, and the pectoralis major is released from its insertion on the proximal humerus. The neurovascular bundle is identified and protected. If the coracoid is to be resected with the glenoid, the pectoralis minor, coracobrachialis, and short head of the biceps are released. If the coracoid will remain, only the biceps and coracobrachialis muscles are released. The musculocutaneous and axillary nerves are very close to

the area of resection and must be protected. The subscapularis tendon is released and the shoulder joint is opened anteriorly. This is followed by circumferential capsular release. The subscapularis is elevated from the undersurface of the scapula, and the osteotomy is performed. The glenoid is then pulled anteriorly, and the posterior muscles are released.

Alternatively, a second posterior incision is utilized to mobilize the deltoid muscle and to expose the posterior aspect of the joint and the glenoid. This permits an accurate osteotomy of the scapula.

Reconstruction

The humeral head can be suspended from the remaining scapula and clavicle as previously described for prosthetic reconstruction following Type V resections (see Dual suspension technique). An arthrodesis is another alternative.

DISCUSSION

The Tikhoff–Linberg resection (Type IV) and its variants, total scapulectomy (Type III), and partial scapulectomy (Type II) are illustrated. Most patients with tumors of the scapula can be treated with these methods; a stable shoulder can be restored and a functional hand and elbow can be preserved (Figure 34.6). All of these procedures are performed through a combination of an anterior and a posterior approach.

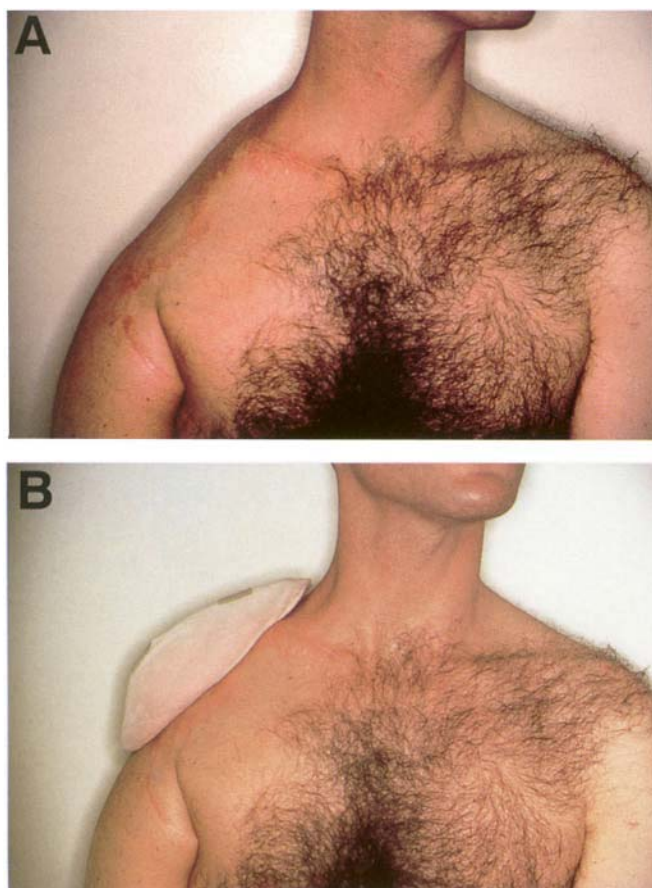


Figure 34.6 (A) Clinical photograph following a Tikhoff–Linberg (Type IV) resection without scapular replacement. (B) Cosmesis can be re-established with a simple shoulder pad attached to the patient's shirt. (Clin Orthop Rel Res no 267 June 1991 pp. 33–41)

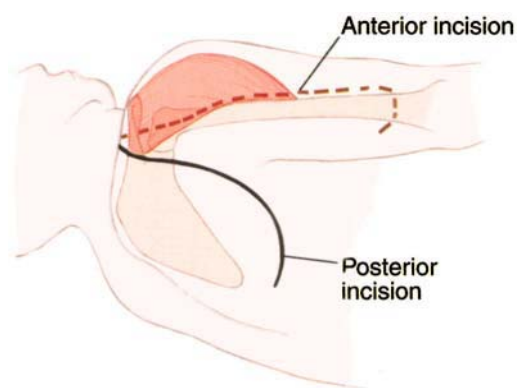


Figure 34.7 Incision. An anterior/posterior approach is utilized. The patient is placed in a lateral position with the affected extremity prepped and draped free. The operative procedure begins with the posterior approach to mobilize the scapula and to explore the retroscapular area to determine if there is any underlying involvement of the chest wall. The anterior approach is utilized following the posterior incision to mobilize the axillary vessels and nerves from any extra-osseous component of the tumor. It is unusual to perform a Type III or Type IV scapular resection from the posterior approach alone unless there is minimal soft-tissue extension.

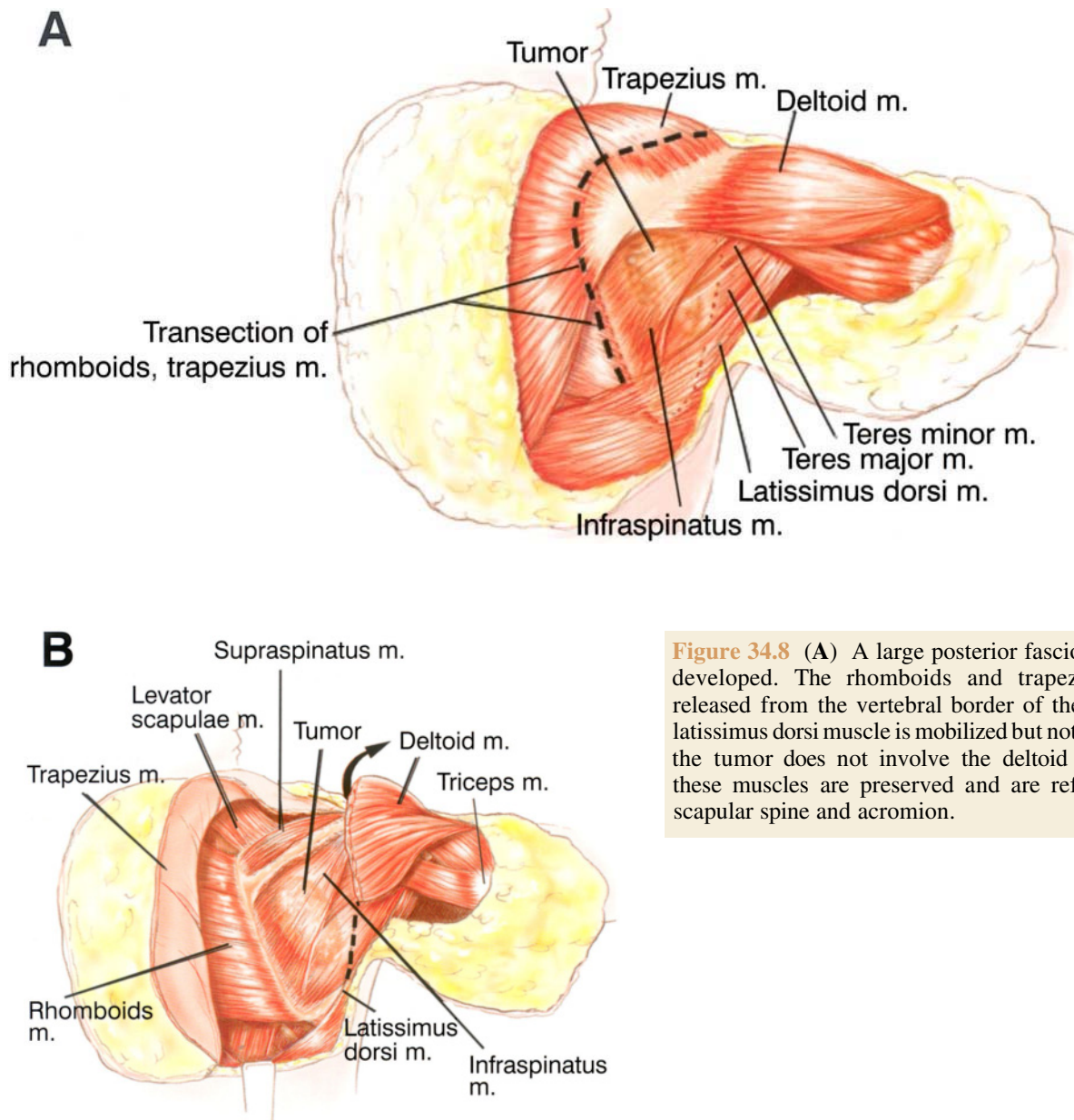


Figure 34.8 (A) A large posterior fasciocutaneous flap is developed. The rhomboids and trapezius muscles are released from the vertebral border of the scapula and the latissimus dorsi muscle is mobilized but not transected. (B) If the tumor does not involve the deltoid or the trapezius, these muscles are preserved and are reflected off of the scapular spine and acromion.

The major differences are the status of the glenohumeral joint and the amount of muscle and bone resected. A total scapula replacement can only be performed under strict criteria when there are significant remaining muscles (see above).

THE TIKHOFF-LINBERG RESECTION, PARTIAL AND TOTAL SCAPULECTOMY, AND TOTAL SCAPULAR REPLACEMENT (Figures 34.7–34.13)

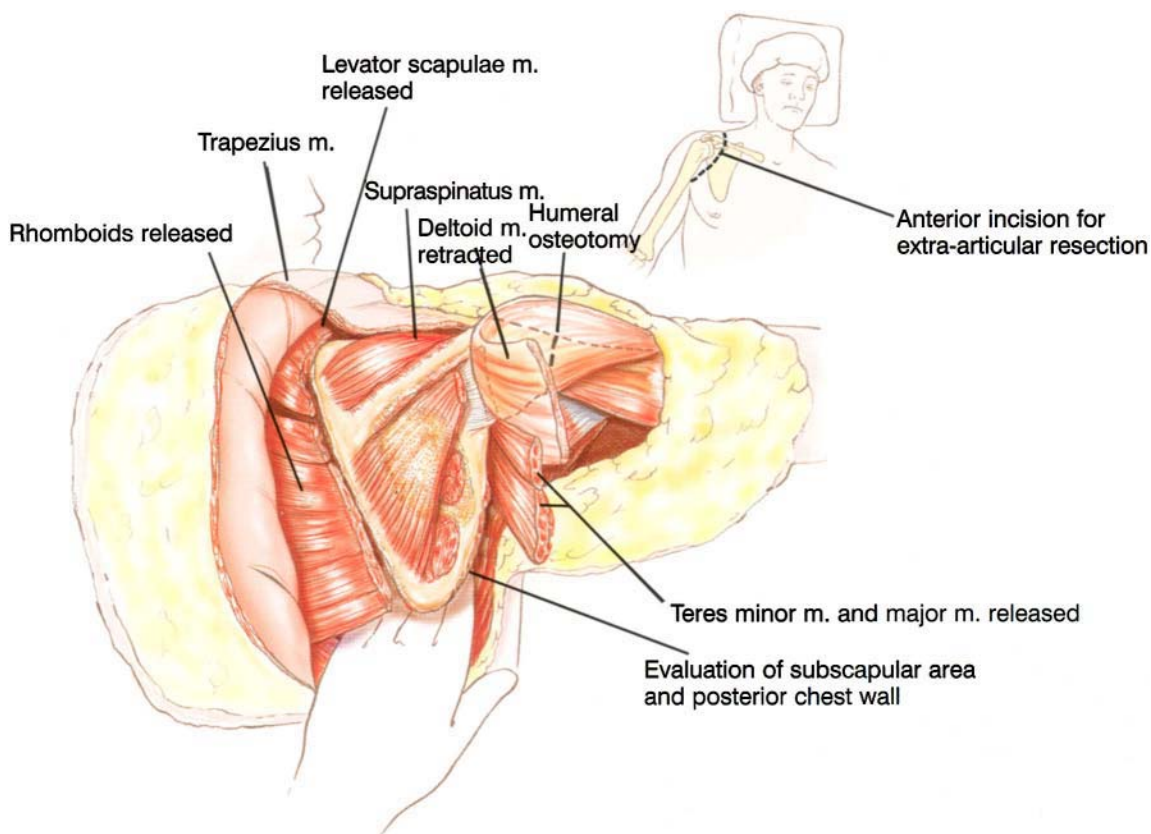


Figure 34.9 Release of periscapular muscles. The rhomboids, infraspinatus, levator scapulae, teres major, teres minor, and triceps muscles are released from the scapula. The margin of muscle that must remain on the scapula depends on the extent of the tumor. A 1–2 cm cuff of muscle is required for most tumors. The deltoid and the trapezius muscles are reflected. If there is no tumor involvement, then they are preserved. Insert shows the anterior incision for mobilization of the axillary vessels and brachial plexus when there is a large soft-tissue component. This incision is routinely used if an extra-articular resection is to be performed; that is, a true Tikhoff–Linberg resection (Type IV). The classical Tikhoff–Linberg resection does not preserve the deltoid or trapezius muscles; however, in order to provide adequate soft-tissue coverage for the scapular prosthesis, these muscles must be retained. Therefore, a modified Tikhoff–Linberg (Type IV) resection is performed.

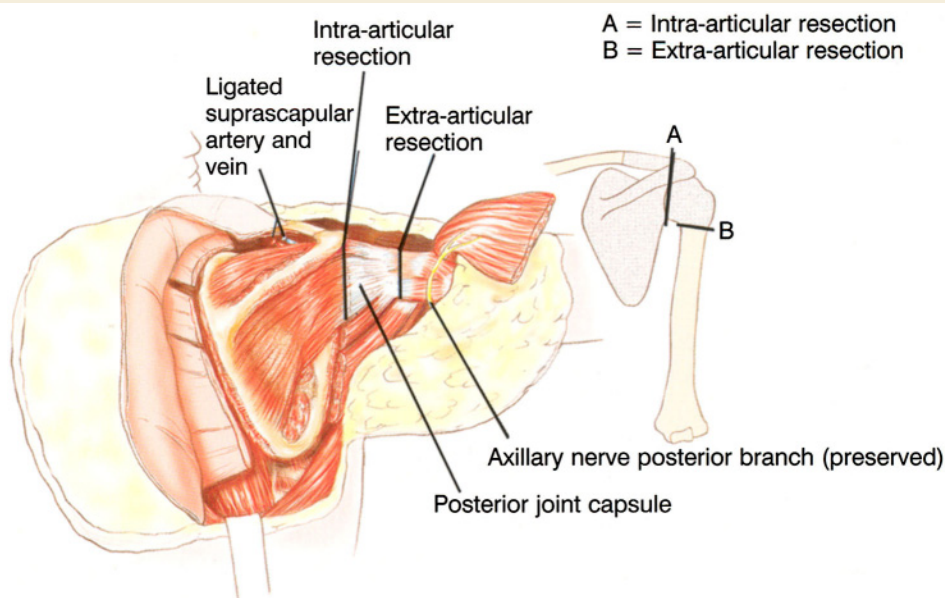


Figure 34.10 Complete release of the scapula following an intra- or extra-articular resection. The insert shows the levels of an intra-articular resection and extra-articular resection. An osteotomy below the humeral head, i.e. a scapulectomy and extra-articular resection of the glenohumeral joint in conjunction with the scapula, is a classical Tikhoff–Linberg resection (Type IV). The determination of either a scapulectomy or a Type IV resection is made intraoperatively.

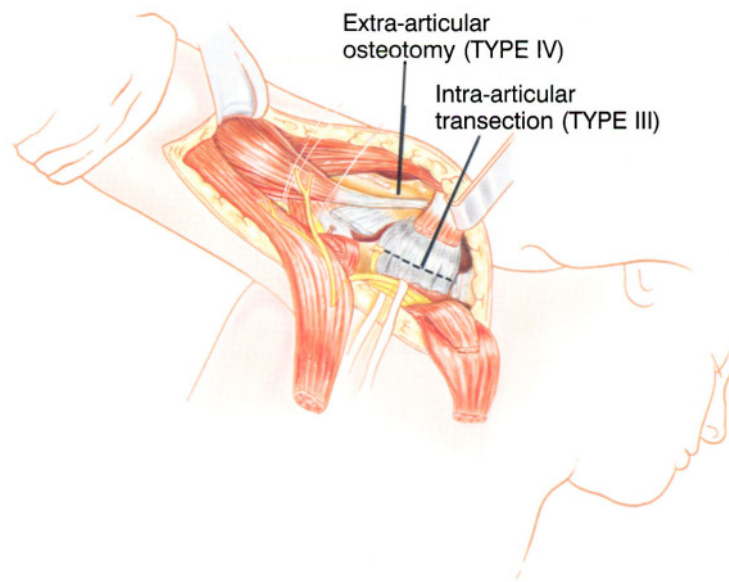


Figure 34.11 Anterior approach and vascular exploration. Most high-grade tumors of the scapula with an extrasosseous component require mobilization of the axillary vessels and the adjacent brachial plexus anteriorly in order to permit a safe resection. This incision is the anterior component of the utilitarian shoulder incision as described in Chapter 9. The pectoralis major is released from the humerus to expose the neurovascular structures. An extra-articular resection is performed by an osteotomy inferior to the glenohumeral capsule. An intra-articular resection (Type III resection) is performed by an intra-articular incision.

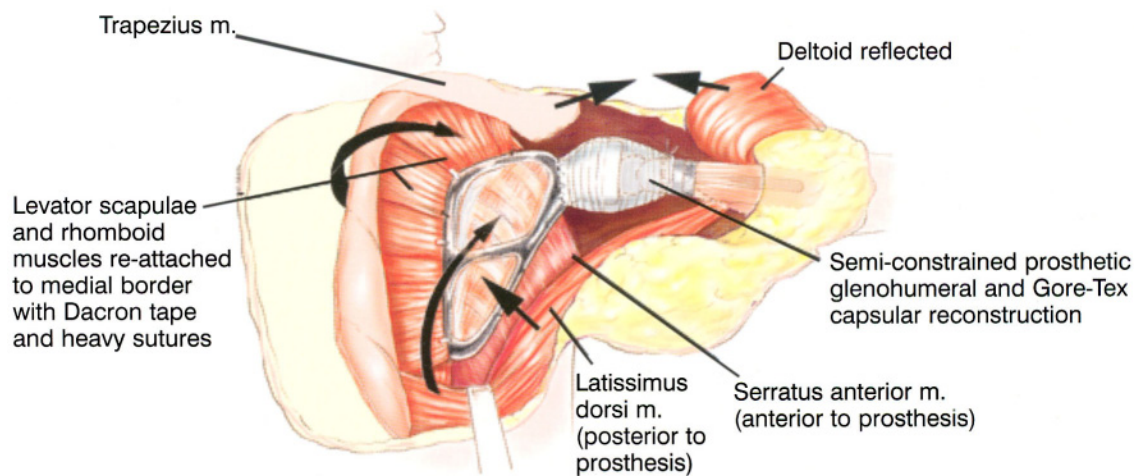


Figure 34.12 Posterior approach and prosthetic reconstruction. If there are significant remaining muscles following a Type III or IV shoulder girdle resection, then a scapula prosthesis is utilized. The scapula prosthesis is centrally fenestrated to permit tenodesis of the muscles to each other (serratus anterior to the rhomboids, latissimus, and trapezius). It also has holes drilled along the axillary and vertebral borders for fixation with Dacron tapes. The deltoid and trapezius muscles must have been preserved as well as the latissimus dorsi in order to perform a scapula prosthetic replacement. The scapula prosthesis is sutured first to the rhomboid muscles with Dacron tape, and then the latissimus dorsi is rotated over the body of the scapula prosthesis and sutured along the vertebral border. The humeral component is then inserted into the osteotomized proximal humerus. A Gore-Tex graft is utilized to reconstruct the capsular mechanism (Figure 34.5). The Gore-Tex is sutured to the proximal humeral prosthesis and the glenoid neck on the scapular prosthesis with 3-mm Dacron tape. The muscle closure consists of tenodesis of the deltoid to the trapezius and the latissimus to the rhomboids and to the serratus anterior muscles. The scapula prosthesis fits between the serratus anterior and the latissimus dorsi and rhomboid muscles "as if in a sandwich".

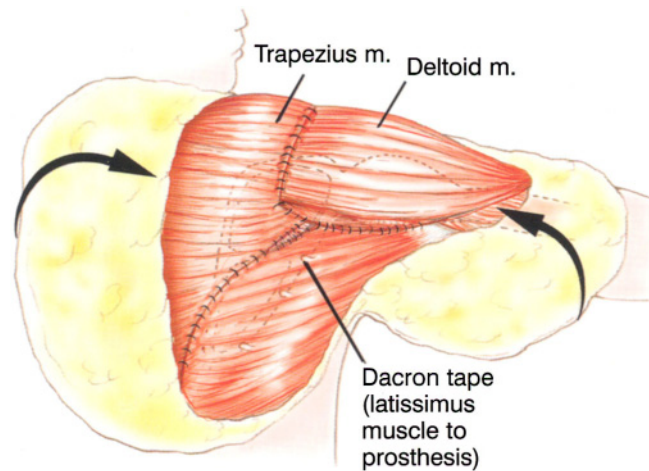


Figure 34.13 Final muscle closure. The deltoid and trapezius muscles have been preserved and are tenodesed together. The latissimus dorsi is rotated up to the lower border of the deltoid and to the rhomboid muscles. The latissimus is sutured to the holes in the axillary border of the scapula prosthesis and the adjacent musculature using Dacron tape and ethibond sutures, respectively. Postoperatively, a 28-gauge chest tube is used for drainage. The arm is held in a sling for approximately 2 weeks. Epineural catheters for postoperative marcaine infusion are routinely utilized (see Figure 34.5E).

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Anesthesia and Perioperative Pain Management for Limb-sparing Surgery

Avi Weinbroum, Nissim Marouani, Eric Lang, David Niv, James Wittig and Valery Rudick

OVERVIEW

Anesthesia and perioperative pain control of patients, who are scheduled to undergo a limb-sparing surgery, necessitate an individualized pain control protocol. It is tailored according to the extent and duration of surgery, as well as requirements of the immediate postoperative patient care. Effects of preoperative chemotherapy and radiation therapy must also be evaluated and considered. The intraoperative use of regional anesthesia, either alone or in combination with general anesthesia, and postoperative use of regional anesthesia and patient-controlled analgesia using the intravenous or epidural routes, are emphasized.

THE ANESTHESIOLOGIST AND THE ONCOLOGICAL PATIENT

Anesthesiologists become involved in the care of patients with malignant disease whenever such patients require pain relief. This involvement may occur at any stage in the disease process. During the perioperative phase, for example, it is the anesthesiologist who develops the patient's individualized pain-control protocol. For patients who require surgery the anesthesiologist is a pivotal member of the team who determines the extent and timing of surgery. Safe intraoperative care of the oncological patient poses a number of challenges to the anesthesiologist. First, tumors are accompanied by widespread pathophysiological changes caused by the physical and mental stress associated with a sudden need for major surgery. In addition, a variety of side-effects may accompany synergistic treatment protocols (i.e. radiotherapy and chemotherapy) that are used to bring about optimal regression of the tumor prior to surgery. Aggressive surgical applications may often require long-term anesthesia, prolonged postoperative analgesia, or even admission to an intensive-care unit.¹

GENERAL CONSIDERATIONS

Because of the variety of disorders that accompany cancer in general, and sarcomas in particular, assessment of baseline and psychological condition of the patient, and optimizing his or her status prior to surgery, are a fundamental priority of the anesthesiologist. Information can be obtained from the patient and the family, the medical records, the attending physician, or a physician–consultant. These patients have invariably already undergone some investigational workup and conservative treatment by the time they are first seen by the anesthesiologist. Many patients with sarcoma are young and rarely suffer from age-related illnesses such as ischemic cardiac disease or hypertension.

Respiratory or behavioral disorders, by contrast, are more common and may exist in association with previous treatment (chemotherapy, immunosuppressive therapy, or radiotherapy), metastasis, or previous surgery. In these cases it is important to assess any existing limitations as would be appropriate for any chronic disease, using the patient's ASA physical status.

PERIOPERATIVE CONSIDERATIONS

Patient Evaluation and Preparation

It is vital to evaluate the patient's initial condition in order to ensure the best outcome (Table 35.1). The diagnosis of a malignancy and the necessity for surgery

Table 35.1 Preoperative collective concerns and complications in the cancer patient

Weight loss, anorexia
Fever, chills, sweats
Dehydration
Weakness, fatigue
Coagulopathy
Anemia, polycythemia
Thrombocytopenia, dysfunctional platelets
Adrenal insufficiency
Ectopic hormone production
With chemotherapy/radiation treatment:
Autonomic neuropathy
Gastroparesis
Tachycardia, dysrhythmias
Orthostatic hypotension
Electrolyte imbalance
Hyperuricemia
Pericardial effusion and tamponade
Cardiomyopathy
Cardiac failure
Neuromuscular abnormalities
Ureteral obstructions
Nephrotic syndrome
Tumor lysis syndrome
Superior vena cava syndrome
Spinal cord compression syndrome
Brain metastases
Mental status changes

may understandably induce a heightened level of anxiety, nervousness, or feelings of denial and rage in an otherwise healthy patient, especially a teenager and his or her family. Patients may ask numerous questions and require intensive psychological support. Some may need anxiolytic drugs. For patients who appear apathetic or depressed, and wish no verbal contact or explanation of what to anticipate, anesthetic drugs may not be required. Prior chemotherapy or radiation, combined with symptoms of organ dysfunction, put an additional burden on the patient. Finally, the patient may also be threatened by the idea of anesthesia. The anesthesiologist should confer with the patient for as long as required to reduce his or her anxiety, and should offer candid explanations of the planned anesthesia, perioperative care, and the selected option of postoperative pain control. Appropriate preoperative medication is also useful for most patients.

Unless brain metastases are present neurological symptoms are rare with sarcoma. These symptoms include headache, nausea, dysphagia, abnormal sensations (e.g. dysesthesia or paresthesia), visual disturbances, loss of sensation, and motor dysfunction.

Results of the neurologic examination should be available to the anesthesiologist, as should results of the peripheral electromyography and computed axial tomography (CAT) of the brain. The anesthesiologist should meticulously evaluate the mobility and function of the neck, mouth, throat, and muscles of the upper extremities.

The cardiovascular system may be involved in tumors or metastases, or obstruction of the inferior or superior vena cava (vena cava compression syndrome). The patient's history may contain signs and symptoms of congestive heart failure, including dyspnea or pulmonary edema. Complaints of facial and arm redness or puffiness, or changes in skin color, may indicate superior vena cava syndrome. Objective physical findings might include caput medusae and venous engorgement, edema of head and neck, or a third heart sound (with or without rales over the pulmonary fields). Chest X-rays and echocardiography will provide further information in such cases. A preoperative cardiac stress test and/or angiography should be considered in patients with chest angina. The respiratory system may be involved as a result of a hematogenously disseminated tumor embolus that causes dyspnea, or of chemotherapy or radiotherapy applied to the thorax. Chest films, arterial blood gases, and/or isotope imaging of the pulmonary vascular bed help differentiate among these conditions.

The presence of a neurosarcoma, chondrosarcoma, or osteosarcoma in the abdominal cavity (either intra- or retroperitoneal) may compromise intra-abdominal organ function. Gastroparesis and bowel obstruction may explain complaints of early satiety, pain, or frequent vomiting. Distension of the abdomen may not be noted on physical examination. Plain X-ray films or CAT of the abdomen may then be indicated. Sarcoma of the ampoule of Vater can present with liver dysfunction, as is the case of hepatic metastases. In both cases, liver function tests are warranted. Compression of the ureters by a retroperitoneal tumor is not infrequent and may lead to renal insufficiency and uremia. Kidney function tests and ultrasonic visualization of the renal excretory component may be indicated preoperatively.

Preoperative insertion of an intraureteral catheter to safeguard lumen patency may be necessary in such cases, especially in pediatric patients who require preoperative sedation or anesthesia. The use of contrast media should be discouraged in patients with poor renal function.

Hematological and biochemical profiles are important when evaluating the need for correction of preoperative anemia or coagulopathy. Hyper- or hypo-coagulability states may not be noticeable unless prothrombin time or activated partial thromboplastin

time is measured. The latter can be associated with a moderate degree of anemia, which is a consequence of intestinal bleeding.

Patients suffering from bone loss due to osteosarcoma may show clinical or subclinical signs of hypocalcemia. This condition may be accentuated in the presence of malnutrition or hepatic dysfunction.² Blood levels of both albumin and calcium should be normalized to avoid cardiovascular manifestations of hypocalcemia and pharmacokinetic disturbances of intraoperative anesthetics such as muscle relaxants.²

Patients with cancer experience various types of pain (i.e. acute, chronic, intermittent, continuous). The Task Force on Pain Management of the American Society of Anesthesiologists concluded that half of the cancer patients suffer from chronic pain.³ With more advanced and terminal disease this figure increases to two-thirds. The effect of pain on the individual is variable. Patients with sarcomas usually present with some degree of pain and are already under some sort of analgesic regimen. Moreover, one type of pain may be superimposed on another. Cancer-related pain management commonly starts with non-narcotic agents such as nonsteroidal anti-inflammatory drugs. If the pain does not subside, the next drugs of choice are usually opioids.

The Pediatric Oncology Patient

A child is a difficult patient whose responses to the many procedures associated with cancer therapy are unpredictable. Children may feel physically and psychologically handicapped in comparison with their peers. Frequent courses of chemotherapy and radiotherapy, blood transfusions, and other sources of discomfort from procedures are difficult for them to accept.⁴ It is essential that the anesthesiologist, together with the rest of the surgical team, talk to the pediatric patient using words and concepts that he or she can understand. Prevention of unnecessary distress or suffering, such as prolonged queueing or long fasting hours, is essential.

Young children undergoing an investigational workup (e.g. roentgen imaging) or radiotherapy to reduce a large sarcoma may require sedation or anesthesia in order to keep them motionless during the procedure. An inhalation technique allows for rapid awakening and is preferred to parenteral sedatives such as benzodiazepines. Sevoflurane is ideal for this purpose because of its rapid onset and emergence and lack of pungency.⁵

The Patient with Previous Antitumoral Therapy

The first line of therapy for various tumors at different stages is chemotherapy that interferes with cell

proliferation. The characteristics of several agents that are most frequently used to treat the patient with sarcoma are listed in Table 35.2. The toxicity exerted by these agents and their relevance to the perioperative anesthesia management are directly related to the agent used, the cumulative dose, the damage inflicted on specific organs (including damage caused in the past) and, possibly, cotreatment with synergistic antitumoral agents. The bone marrow, gastrointestinal tract, and blood-circulating elements, all of which are

sometimes associated with ulceration and bleeding in the skin and mucosal layer, are most severely affected by the toxic effects of these agents. Acute or residual pulmonary and cardiac toxicity is also a concern.

Radiotherapy is a second choice of presurgical treatment. The use of powerful, high-precision radiation generators has minimized unnecessary body exposure and the incidence of side-effects such as nausea, vomiting, general sickness, abdominal cramps, and lung tissue changes (Table 35.3). The use of antiemetics

Table 35.2 Preoperative toxicity of selected chemotherapeutic agents

Therapy	Signs and symptoms
Alkylating agents	Nausea, emesis, bone marrow depression, agranulocytosis, anemia, thrombocytopenia, hemorrhagic cystitis, alopecia, uric acid nephropathy
Busulfan, chlorambucil, melphalan	Pulmonary toxicity
Busulfan, cytoxan	Cardiac toxicity
<i>Anesthesia preoperative concern:</i> Cytoxan may cause a prolonged response to succinylcholine due to cholinesterase inhibition	
Antimetabolites	Nausea, emesis, gastrointestinal toxicity with bleeding, diarrhea, dehydration, acute and chronic hepatitis
5-Fluorouracil	Bone marrow depression, megaloblastic anemia, acute cerebellar syndrome, gastrointestinal and hepatic toxicity
Methotrexate	Bone marrow depression, interstitial pulmonary infiltrates, ulcerative stomatitis, renal tubular necrosis, hepatic dysfunction
<i>Anesthesia preoperative concern:</i> 6-Mercaptopurine can cause nondepolarizing muscle relaxant neuromuscular blockade	
Antineoplastic alkaloids	Neurotoxicity with peripheral paresthesia, muscle wasting, loss of deep tendon reflexes
Vinblastine	Bone marrow depression, myelotoxicity, antidiuretic hormone secretion
Vincristine	Ventricular tachycardia, hypo- or hypertension, peripheral neuropathies, bronchospasm
Paclitaxel	Arrhythmias, atrial ventricular block, bone marrow suppression
<i>Anesthesia preoperative concern:</i> Vincristine may elevate potassium secondary to muscle wasting. Use caution with succinylcholine. Laryngeal muscle paralysis can occur	
Anthracycline antibiotics	Bone marrow depression, myelotoxicity, cardiomyopathy with congestive heart failure, decreased left ventricular ejection fraction, biventricular failure
Bleomycin	10% pulmonary toxicity, interstitial fibrosis, renal parenchymal failure
<i>Anesthesia preoperative concern:</i> Bleomycin patients keep at $\text{FiO}_2 < 28\%$ to avoid progressive pulmonary fibrosis and edema. Maintain fluid restriction, monitoring, and colloid administration	
Miscellaneous agents	
Cisplatin	Renal damage with decreased clearance, neuropathy, including stocking/glove paresthesia, areflexia, ocular toxicity and loss of hearing, bronchospasm, cardiac arrhythmias

Table 35.3 Preoperative effects and concerns of radiation therapy

<i>Organ/Function</i>	<i>Acute (up to 4 weeks)</i>	<i>Intermediate (1-3 months)</i>	<i>Late (several months to years)</i>
Skin	Erythema, rash, hair loss		
Gastrointestinal	Malnutrition, anorexia, nausea, emesis, esophagitis, dehydration, gastroenteritis, stomatitis	Bowel adhesions and obstruction, enteric fistula	
Cardiac			Pericarditis, pericardial effusion, fibrosis
Pulmonary			Pleural effusion, fibrosis, pneumonitis, esophageal-tracheal fistula
Hematologic	Bone marrow depression		
Additional anesthesia concerns	Electrolyte abnormalities, fluid volume status	Fluid volume status, ascites with subsequent respiratory compromise	

(e.g. metoclopramine, droperidol, or ondansetron) and a short course of corticosteroids (e.g. dexamethasone or a 5-HT₃ antagonist), plus a dopaminergic antagonist, may alleviate these symptoms.⁶ Since bone marrow suppression may occur after large-scale bone irradiation, a full hematologic profile should be performed prior to surgery.

PREOPERATIVE VISIT AND DRUG ADMINISTRATION

It is important that the patient meet the anesthesiologist prior to surgery. A good relationship may comfort the patient so that mild sedation may suffice prior to commencement of anesthesia. It is good practice not to administer drugs intramuscularly. Oral or rectal administration, or the use of a pre-existing intravenous line, is psychologically and physically less traumatic. These drugs can be administered shortly before the patient is brought into the operating room. Metoclopramide, sodium citrate, and other drugs are highly recommended in patients with gastroparesis or decreased intestinal motility. Ondansetron is the most effective antiemetic for the management of patients receiving chemotherapy or radiotherapy;⁷ it can be administered enterally or parenterally.

Electrolyte and fluids should be administered before surgery by the attending physician and revised, if necessary, by the anesthesiologist. Volume replacement is frequently needed in the oncological patient because

of the decreased drinking, repeated bowel preparation prior to surgery, or the need for relative hyperhydration to ameliorate renal dysfunction. Volume replacement should be performed cautiously in patients with a history of congestive heart failure or ischemic heart disease.

ANESTHESIA

The factors that may have the greatest negative influence on the patient outcome are anemia and thrombocytopenia, immune suppression, and renal or cardiac dysfunction. These must be evaluated pre- and postoperatively. Blood must be available, and antibiotic treatment should be initiated in advance unless a sample from a suspected infected area is to be retrieved for culture and antibiogram. Major surgical procedures such as hemipelvectomy or resection of a retroperitoneal sarcoma, require large-bore intravenous lines as well as arterial lines. Central venous measurement is helpful in assessing changes in circulating blood volume in procedures that cause severe bleeding, and in caring for patients who require good hydration to optimize renal function but also present symptoms of myocardial insufficiency. Patients who are hemodynamically fragile or suffer from cardiac or pulmonary disease may benefit from the insertion of a balloon-tipped intrapulmonary (Swan–Ganz) catheter, which allows judicious administration of volume therapy instead of vasoactive drugs.

GENERAL ANESTHESIA

Special Considerations

Besides standard monitoring (i.e. electrocardiography, noninvasive blood pressure, and pulse oximetry), additional monitoring may be required. The risk of aspiration exists in patients with a large abdominal mass, gastroparesis, or increased intracranial pressure, as well as in those who suffer from postchemotherapy or radiation sickness. One way to reduce this risk and provide good anesthesia is to apply an epidural or spinal block. If general anesthesia is indicated, it should be carried out cautiously. The airway should be protected with the Selick maneuver or by awake intubation, preferably after the stomach has been emptied. Caution should be paid in patients with cardiac dysfunction (post-chemotactic, radiation, or postischemic) or myocardial involvement due to a myxoma. Patients with hypovolemia (caval compression syndrome) may be hemodynamically unstable. Profound hypovolemia is a contraindication to centroneural regional anesthesia.

Maintenance of Anesthesia

There are no contraindications to the use of any anesthetic drug, either inhalation or intravenous, in patients with sarcoma. Patients with altered organ function may exhibit clinically significant abnormal responses to some drugs, especially those that depend on hepatic metabolism or renal excretion. Large tumors may bleed and require replacement of 2–4 units of blood. Hemodilution can decrease the rate of intraoperative blood loss and the necessity for controversial allogenic blood transfusion;⁸ however, it could lead to hemodynamic instability, especially in patients with preoperative anemia or autonomic system deficiency. During prolonged major surgery (e.g. hemipelvectomy), the effects of prolonged intravenous or inhalation anesthesia may become clinically apparent. An intravenous drug infusion will result in a lower cumulative drug dose than repeated boluses.⁹

Various drugs can be used for induction and maintenance of anesthesia in the oncology patient. Their common characteristics are the ability to induce complete amnesia and a rapid onset of deep sedation or hypnosis and the ability to be synergistic with other intravenous or inhalation agents. Propofol has a rapid onset and recovery and can be used by infusion. It also exerts some antiemetic effect and has fewer side-effects than other general anesthetics. However, caution should be paid when propofol is administered to patients who are hypovolemic, hemodynamically unstable, or who suffer from hepatic dysfunction.¹⁰ Midazolam, a water-soluble benzodiazepine, is frequently used

during induction and maintenance of anesthesia for short-lasting procedures, interventions that require monitored care anesthesia, or chemotherapy sessions in children. The subsequent central respiratory depression is not as profound as that following opioids or hypnotics, although recovery is somewhat prolonged.¹¹

During the past 10 years isoflurane has almost completely replaced halothane. Isoflurane is frequently used for maintenance of anesthesia in both adults and children. Sevoflurane is a novel inhalation agent that produces virtually no upper-airway irritation, even when given at a high minimal alveolar concentration (MAC).⁵ It is an excellent agent for pure inhalation induction in children, as well as for maintenance in patients of all ages. Nausea and vomiting are less frequent in patients who have received sevoflurane than in those who receive desflurane or isoflurane.¹² Because it is quick and smooth both during induction and recovery, sevoflurane is a good choice for short chemotherapy or radiotherapy sessions in children, especially when intravenous lines are unavailable prior to the intervention. Nevertheless, agitation can ensue following administration of this agent, especially in the pediatric population, and particular attention must be paid to patients who have received sevoflurane. During the immediate postanesthesia period, low-dose midazolam can control the agitation.¹¹ Desflurane, an inhalation agent with a rapid onset, is especially useful for ambulatory surgery. It is not recommended for induction in the pediatric population because of its association with a high incidence of coughing and laryngospasm.¹³

Muscle relaxants are used in combination with other anesthetic drugs. The new short-acting drugs have fewer side-effects and provide better manageability and the possibility of prompt cessation of general anesthesia. These include atracurium, vecuronium, mivacurium, and rocuronium.

Opioids, including fentanyl, sufentanyl, alfentanyl, and remifentanyl, are frequently used during anesthesia. Sufentanyl is one of the most widely utilized drugs because of its rapid onset time and short elimination, half-life.¹⁴ It is seven to ten times more potent than fentanyl. Because it does not accumulate within the body, sufentanyl is the drug of choice in prolonged surgical procedures. Remifentanyl is a novel, extremely short-acting opioid that is metabolized by pseudocholinesterase. Its half-life is approximately 10 minutes. Alfentanyl is a short-acting opioid with a rapid onset. Its duration of action is two to three times shorter than that of fentanyl; however, this property also limits the drug's postoperative analgesia efficacy. Pharmacokinetically, alfentanyl is one of the few opioids indicated for day surgery.¹⁴

Oncological patients are more prone than other patients to develop pulmonary embolism and regional thrombosis in the postoperative period. This is because of circulating procoagulation factors, such as tumoral debris and their overturned fragments, or prolonged surgery.¹⁵ Prophylactic anticoagulation with low-dose or low-molecular-weight heparin, may prevent these complications.¹⁶ The risk-to-benefit ratio of performing a neural block in a partially anticoagulated patient is debatable. Continuous infusion of local anesthetics and/or opioids in a preinserted epidural catheter is not contraindicated by the anticoagulant treatment; however, in the presence of altered coagulation tests, the insertion or removal of the catheter is not practicable.¹⁷

REGIONAL ANESTHESIA

Regional anesthesia is useful for small-to-medium-size surgical procedures; however, the oncological patient may need to be well sedated with propofol or midazolam. In pediatric patients, and patients in whom surgery of a large area is planned, however, this will not suffice, and a combined anesthesia regimen (regional and general) is recommended. Combined anesthesia enables one to use smaller amounts of intravenous analgesics and opioids than are used during general anesthesia. Moreover, the patient awakens faster and has minimal systemic side-effects.

CENTRAL BLOCKS

An epidural (cervical, thoracic, lumbar) block is accomplished by inserting a catheter into the extradural space through which local anesthetics and/or opioids are administered intermittently or continuously. This technique requires smaller quantities of opioids than the intravenous route. In addition, postoperative shivering is less than that associated with emergence from general anesthesia. This is particularly beneficial to the patient with cardiac disease.

Caudal block is particularly useful in the pediatric population, especially in very young children.¹⁸ The trans-sacral approach is an epidural block in the sacral region. The catheter/needle is inserted between the first and second or the second and third sacral vertebrae at the horizon line that joins the interfaces of the two vertebrae and the level of the posterosuperior iliac crest.

Spinal block is effective for relatively short or medium-length procedures. It requires one-tenth of the volume needed for an epidural block. When morphine is added intrathecally, postoperative pain control can last up to 24 hours.¹⁹

PERIPHERAL BLOCKS

Upper-limb blocks include several approaches that cover various anatomic areas depending on the site of surgery (Tables 35.4 and 35.5), the surgeon's preference, and the possible requirements for continuous pain control. The following paragraphs summarize general considerations regarding various blocks.

Interscalene Block

Interscalene blocks usually provide good anesthesia for procedures of the upper extremity. They are a poor choice for surgery on the medial aspect of the arm and forearm because the inferior cord, which leads to the ulnar nerve, may not be blocked.

One should be careful to avoid injecting the local anesthetic into the epidural or intrathecal space, or into the vertebral artery. Proper needle placement and careful aspiration before injection of the local anesthetic limit the incidence of such complications. The needle should be directed medially, caudally, and posteriorly.

Brachial Plexus Blocks

The interscalene, supraclavicular, or infraclavicular techniques can block the brachial plexus. This habitually leads to a motor block earlier than a sensory block.

Subclavian Perivascular Brachial Plexus Block

This block provides sensorial loss identical to that offered by the subclavian block. When performing this block the anesthesiologist must bear several points in mind:

1. A puncture of the subclavian artery is common.
2. There is a risk of puncturing the lung and causing a pneumothorax. This risk can be reduced by using a short (1½-inch) needle.
3. This block may also block the stellate ganglion.
4. The phrenic nerve might be involved in the block.
5. A hematoma may occur.
6. The needle may contact the plexus before it reaches the rib.

Infraclavicular Approach of the Brachial Plexus

This approach is useful for surgery of the forearm. The roots generate the following nerves:

1. Lateral aspect of the musculocutaneous nerve C5–7
2. Anteromedial aspect of the median nerve C6–T1
3. Ulnar nerve C8–T1
4. Posterocutaneous nerve of the forearm C5–C8
5. Mediocutaneous nerve of the forearm C8–T1

Table 35.4 Choice of blocks for upper extremity surgical procedures

	<i>Interscalene</i>	<i>Perivascular subclavian</i>	<i>Infraclavicular</i>	<i>Axillary</i>
Arthroscopy of shoulder	+			
Closed reduction dislocation of shoulder	+			
Total shoulder replacement	+			
Resection distal end clavicle	+			
Arthroplasty of shoulder for chronic dislocation	+			
Elbow surgery		+	+	+
Ulnar nerve transposition		+	+	+
Open reduction internal fixation (ORIF) olecranon		+	+	+
Procedure on fourth and fifth digits		+	+	+
Excision distal end of ulna		+	+	+
Carpal tunnel release	+	+	+	+
deQuervain's release	+	+	+	
Volar ganglion resection	+	+	+	+
Dupuytren's contracture				+
Excision ganglion dorsum wrist		+	+	
Radial collateral ligament repair	+	+	+	
Arthroplasty of thumb	+	+	+	
Open reduction internal fixation (ORIF) fracture radius	+	+	+	
Excision distal radius	+	+	+	
Procedure on digits			+	

Table 35.5 Choice of local anesthesia for the upper extremity

<i>Area and nerve origin</i>	<i>Blockade approach</i>
Shoulder	
C3–4, C5–6	Interscalene
Elbow	
C5–8, T1–2	Infraclavicular
Medial aspect C8, T1–2	Subclavian perivascular
Lateral aspect	
Posterolateral aspect C5–8	
Forearm	
C5–7 Musculocutaneous nerve	Infraclavicular
C6–T1 Median nerve	Subclavian perivascular
C8–T1 Ulnar nerve	
C5–8 Posterior cutaneous nerve	
C8–T1 Medial cutaneous nerve (radial nerve) and median nerve	
Wrist and hand	
Wrist snuffbox Median nerve	Subclavian perivascular
Radial nerve	
Musculocutaneous nerve	Interscalene
Hand and digits	
Ulnar and digits	Axillary
Median nerve decompression	

Surgery of the forearm region requires the blockade of all the branches originating from the brachial plexus; anatomically, the C5–8–T1 nerve roots form the latter. The block of choice of the brachial plexus can be easily achieved by the infraclavicular approach. It provides anesthesia for surgery of the forearm region because it can block all the nerves involved in this area.

Surgery at the base of the thumb requires anesthesia of the median, radial, and musculocutaneous nerves. Such anesthesia is provided by the infraclavicular approach. The latter two nerves might be missed when using the axillary approach (see below). Although the infraclavicular, interscalene, and subclavian perivascular approaches to the brachial plexus block are equally good techniques for surgery at the base of the thumb, the infraclavicular approach is particularly beneficial when used in a continuous mode by the insertion of an epidural catheter.

Axillary Approach to the Brachial Plexus Block

For this block the patient must adduct the arm by 90°. This may pose a problem in patients with limited shoulder motion (e.g. individuals whose shoulder is affected by rheumatoid arthritis). This block provides good anesthesia for surgery on the hand and wrist, especially in the area of the ulnar nerve distribution. It may not provide good anesthesia to the area supplied by the radial nerve in the lateral aspect of the hand and forearm. This approach also may not block the musculocutaneous nerve, which innervates the snuffbox. Another limitation of this block is that it usually does not provide anesthesia to the region above the elbow, even though it may be effective at the elbow itself. The brachial plexus block achieved by the axillary technique provides a greater sensory block and a poorer motor block than the other earlier-described approaches.

Surgical procedures at the wrist and the hand which may be done under an axillary block include median nerve decompression (carpal tunnel syndrome), excision of ganglia tendon, nerve repair, and reduction/fixation of small fractures.

Humeral Canal Nerve Block

Patients who are unable to abduct an arm, and who need a block of the brachial plexus at the arm and wrist distribution, may benefit from a humeral canal nerve block. This block is useful for all interventions done under the axillary block approach, and it anesthetizes that region to some degree. The needle is introduced next to the brachial artery at the mid-length of the arm, and the various nerves (ulnar, median, and radial) are identified with a nerve stimulator.

Block of the Lower Limb: its Nerves and Dermatomes

Psoas Block

The psoas (paravertebral) block is an efficient way to treat chronic pain of the lower limb. It is also useful perioperatively, because continuous pain control can be achieved by the administration of local anesthetics (with or without opioids) via a continuous epidural catheter. The lumbar plexus is formed by the ventral rami of the first, second, third, and major parts of the fourth lumbar nerves. It is located deep in the psoas major muscle, in a kind of compartment formed by the muscle and its fascia anteriorly; the bodies of the lumbar vertebrae medially; and the transverse process of the same vertebrae, the intertransversal ligaments and muscles, and the quadratus lumborum muscle posteriorly.

A group of nerves innervating the upper segment of the lower limb lies in close proximity to the line between the fourth and fifth lumbar vertebral transverse processes. They run from laterally to medially and include the lateral-cutaneous nerve of the thigh, the femoral nerve, the genitofemoral nerve, the obturator, and the lumbosacral trunk. In orthopedic oncology patients the psoas block is mainly used for hip prosthesis, total hip replacement, patellectomy, leg amputation (above- or below-knee), tibial plating, and operation on the toes, including ankle open reduction and internal fixation (ORIF).

Three-in-one Block

This distinctive block was first postulated by Winnie and applied by Lonsdale.²⁰ It consists of administering an abundant volume of local anesthetic below the fascia iliaca in order to block all nerves composing the lumbar plexus. The application of this block requires that one draws an imaginary line between the anterosuperior iliac crest and the symphysis pubis point. At one-third of the distance between the iliac crest downward and 1 cm below the line, the needle is introduced at a 90° angle to the skin. The femoral nerve can be blocked completely, but there is only a 90% success of anesthetizing the laterofemoral cutaneous nerve and a 75% success in the obturator nerve. The lumbar plexus is entirely blocked only in about 60% of the patients, especially the genitofemoral ramus.

The femoral nerve block is effective for femoral bone surgery or biopsy in the anterior region of the lower limb. It is the most important and extensive peripheral nerve block of the lower limb, especially when combined with the psoas block. In such occasions the neural and muscle masses are completely anesthetized.

Sciatic Block

The sciatic nerve originates from L4–5, S1–3 roots. It innervates the posterior part of the thigh and all areas below the knee joint except the medial aspect up to the medial malleolus, which is supplied by the saphenous nerve. The sciatic block affects the sensory part of the sciatic nerve and its rami and allows operating only on the foot.²¹ More extensive operations require additional nerve blocks, such as a femoral or an obturator nerve block. The sciatic block is frequently used to obtain perioperative analgesia. There are three different approaches to this block: anterior, posterior, and lateral. Each is easy to perform and is almost always successful. To apply this block the patient is placed on the bed in the Sims position on the side opposite to the one to be blocked. The hip and knee are flexed, and the knee on the side to be blocked should cross over the body and touch the bed.

The block landmark is the line between the posterosuperior iliac crests and the greater trochanter.

Distal Block of the Lower Limb

The distal block is useful when preparing for a small-size procedure or when the patient is fragile and general anesthesia is unacceptable.

PHANTOM LIMB PAIN AND SENSATION

Ambroise Pare first described phantom limb pain after Lord Nelson had lost his arm at the Tenerife battle in 1797. The patient immediately or some time after the limb amputation can feel both sensation and pain. The authors refer to both symptoms as "phantom pain"; for information regarding the distinction between the two, see Herd's review.²² None of the theories attempting to explain the phantom phenomena has been entirely satisfactory. Most researchers suggest that this kind of pain arises in the residual parts of the peripheral sensory neuron;²³ others contend that it originates from within the central nervous system.²⁴ It may also be a product of a neuropsychological process representing a sort of unconsummated mourning for the lost body part.²⁵

Phantom pain may appear spontaneously; however, in most cases a local or remote stimulus triggers it. The pain may appear immediately after amputation, but there is habitually a short period of latency. Psychological or visceral stress (e.g. urination or defecation) can also give origin to such pain. The intensity of phantom pain is directly proportionate to the severity and duration of pain endurance before the amputation or the degree of perioperative-related psychological distress.²⁶ Although the severity of pain usually

decreases over a period of years, it may reappear after years of absence.

Conservative treatment such as the classic analgesics (e.g. paracetamol, nonsteroidal anti-inflammatory drugs, propoxyphene, or even morphine) are generally ineffective to control phantom pain, and their prolonged use may bear many side effects. These drugs are coadjuvated with tricyclic antidepressants (e.g. amitriptyllin), anticonvulsives (e.g. depakin), neuroleptics (e.g. halidol). The concomitant perineural injection of local anesthetics such as of lidocaine, the use of transcutaneous electrical nerve stimulation, or ultrasound are also options for phantom pain control. Regional analgesia (e.g. epidural block) is another alternative. Finally, psychological treatment, relaxation, biofeedback, hypnosis, and various complementary methods such as auriculotherapy and acupuncture are acceptable tools.^{24,27}

Several institutions also use invasive methods of pain control in these patients. These include spinal cord stimulation and the interruption of the nerves from the periphery to the cortex. Surgery is used only for treating highly resistant phantom pain.²⁸

PERINEURAL ANESTHESIA

Perineural anesthesia is effective in controlling post-operative pain and reducing narcotic requirements following limb-sparing resection or amputation. In our experience it has also been effective in preventing phantom limb pain. It can be utilized in all anatomic locations. During limb-sparing resection or amputation all major neurovascular bundles are routinely exposed; thus they are easily amenable to perineural anesthesia. During surgery, prior to wound closure, each major nerve sheath is opened. A 20-gauge Silastic epineural catheter is threaded proximally at least 5 cm in the nerve sheath. The sheath opening is closed around the catheter using a 4-O absorbable suture, being sure to anchor the catheter securely. This is performed for each major nerve that has been exposed during the surgical procedure. Catheters are externalized through separate stab wounds made in the skin with a 16-gauge angiocath and stitched in place. Following limb-sparing resection the patient is awakened from anesthesia, and neural integrity is checked in the operating room. Immediately following a baseline neurological examination, a 10–20 ml bolus of 0.25% bupivacaine is delivered into each catheter. For amputees the bolus is given prior to awakening from anesthesia, since good perioperative pain control is believed to prevent phantom limb pain. The catheters are attached to standard intravenous infusion pumps and the rate is set at 4 ml/h of 0.25% bupivacaine. This rate can be

titrated for optimal pain relief. Catheters are typically left in place for 5–7 days. Some amputees, particularly those with intense and prolonged preoperative pain, are prone to pain-management problems. In these instances perineural anesthesia can be continued as an outpatient using portable infusion pumps, until pain can be adequately controlled with oral medications. **Table 35.6** is a summary of the major nerves exposed and used for perineural anesthesia following limb-sparing resection and amputations.

Several centers have been utilizing perineural anesthesia for all limb-sparing resections and amputations. The procedure is safe and reliable, although there is some risk of systemic toxicity. Typically, adults require 120–240 mg of bupivacaine 0.25% over a 24-h period. Perineural anesthesia can reduce postoperative pain by 90–95% and thus reduce narcotic requirements drastically (~80% reduction).

POSTOPERATIVE ANALGESIA

Maintaining an acute pain-control service requires dedication from the members of the pain management team. They must be available day and night, and respond promptly to any kind of request or call from the nurse, surgeon, patient, or family. Every hospital that treats cancer patients should have a team whose responsibility is to operate the pain-control service. This group includes anesthesiologists and intensivists, surgeons, nurses, psychologists, social workers, and volunteers. All patients having pain problems are introduced to the team. With the attending physician they select the best protocol for the specific patient. Although this decision is made independently from the type of surgery, it must take it into account.²⁹

A successful postoperative pain treatment depends on several factors. First, the surgical team must discuss the plan in detail with the selected family members who must be trained to carry out the plan. The family and patient must comply with the pain-control plan and believe it will serve the patient optimally. Second, an objective person such as an attending nurse must perform pain assessment frequently during the immediate postoperative period. Third, the patient must report his or her pain objectively, without exaggerating or underevaluating its severity. Any side-effects must also be reported. Side-effects may be the first sign of a need to discontinue the mode of

Table 35.6 Major nerves exposed and used for perineural anesthesia

<i>Nerves utilized</i>	
<i>Limb-sparing resection</i>	
Proximal femur	Sciatic and femoral nerves
Caution: avoid vascular pedicle to gluteus maximus in greater sciatic notch	
Distal femur	Sciatic nerve
Proximal tibia	Sciatic nerve
Proximal humerus	Brachial plexus
<i>Amputation</i>	
Hemipelvectomy	Iliolumbar and femoral nerves
Hip disarticulation	Sciatic, femoral, and obturator nerves
Above-knee amputation	Sciatic nerve and percutaneous femoral nerve (placed lateral to the femoral pulse)
Forequarter amputation	Brachial plexus

treatment, change the dosage, or switch to a different drug. The nurse must regularly record the patient's vital signs (i.e. heart rate, blood pressure, respiratory rate and oxygen pulse oximetry) and ensure they remain within acceptable limits in the specific patient. The nurse and the entire team should be prepared to take measures to stop pain treatment when necessary, as well as to initiate resuscitation measures and call for help in emergencies.

It is essential to prescribe the exact dosage and indicate the mode of administration of each drug, as well as to calculate the dose accurately. The oncological patient usually requires a series of repeated procedures following surgery. The aim of a pain-control modality is to attenuate, or even abolish, the pain associated with the treatment. The more compliant the patient is with the pain-control system, and the more appropriate the dosing and type of drug, the stronger the patient will be in undergoing additional therapeutic protocols.

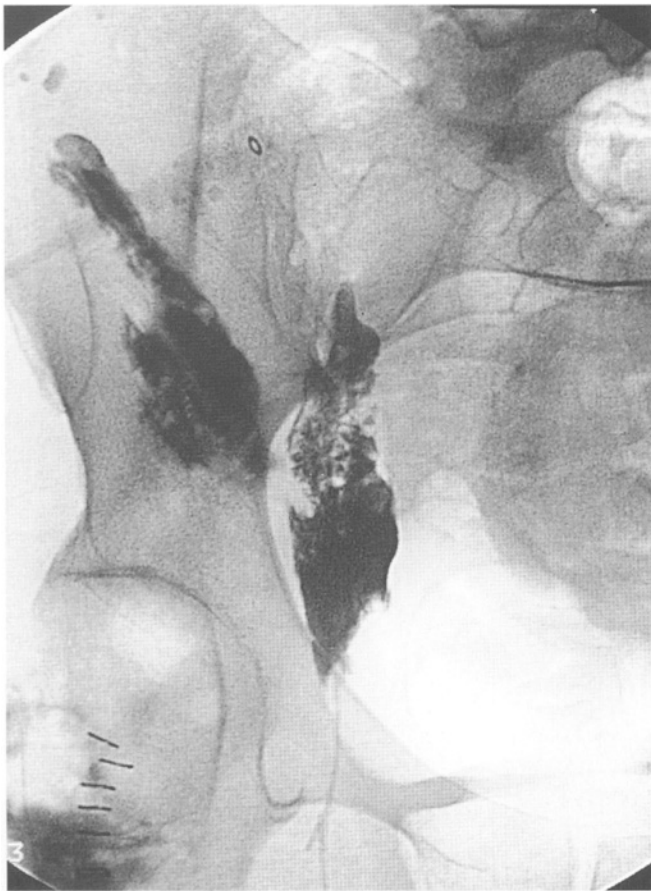


Figure 35.1 Epineural injection following hip disarticulation. Contrast media indicates position of the catheter in the obturator nerve, sciatic nerve, and femoral nerve sheath.

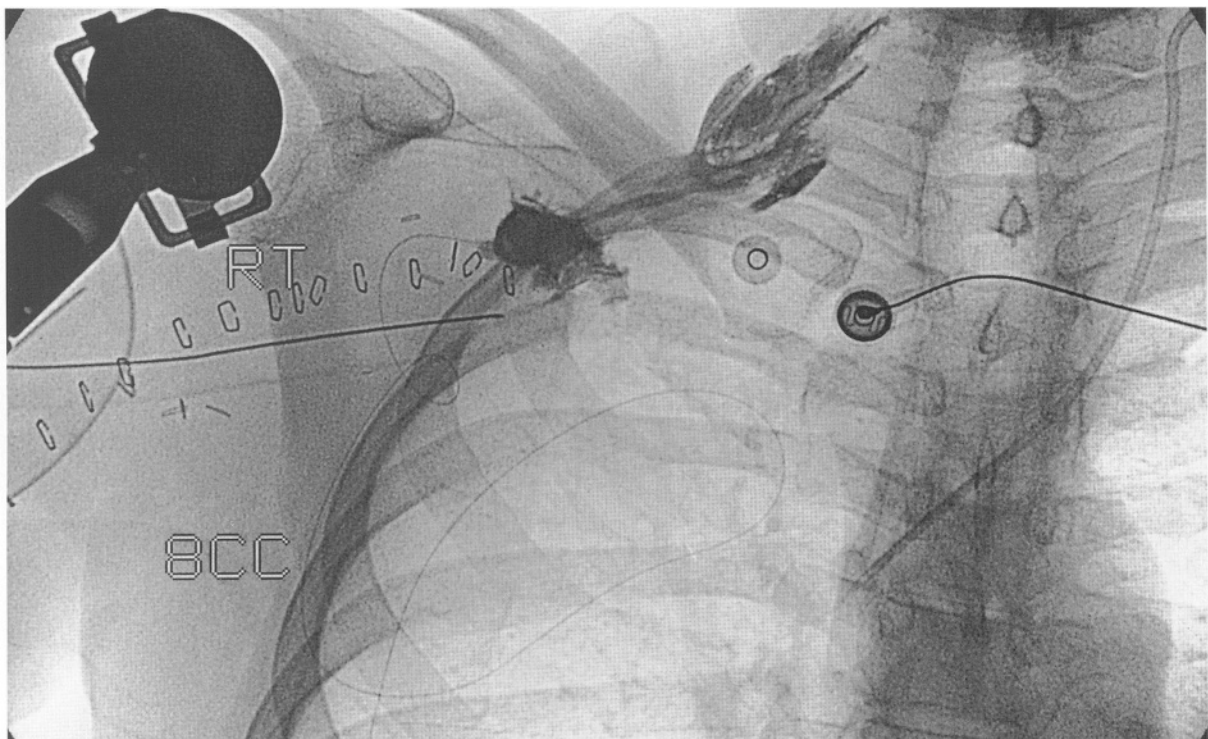


Figure 35.2 Epineural catheter with contrast media in the proximal brachial plexus, following a proximal humeral resection. We use epineural anesthesia routinely following shoulder girdle resections and/or amputations.

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Principles of Rehabilitation after Limb-sparing Surgery for Cancer

Riki Oren, Alice Zagury, Orit Katzir, Yehuda Kollender and Isaac Meller

OVERVIEW

Until around 1970 amputation was the principal operation performed for bone and soft-tissue sarcomas of the extremities, shoulder, and pelvic girdle. Today 85% of these tumors are treated by limb-sparing surgery (LSS), a procedure that involves reconstruction of bones, joints, and soft tissues using endoprostheses, allografts, autografts, and composites. With proper evaluation and surgical management about 60% of these patients are cured of their underlying disease.

This progress creates new opportunities for rehabilitation medicine. The purpose of this chapter is to describe major considerations associated with the rehabilitative care of patients who have undergone LSS. Specific information on surgery, principles of rehabilitation, and incidence of complications is presented for LSS surgery of the distal femur and knee joint, proximal femur and knee joint, proximal humerus and glenohumeral joint, proximal femur and hip joint, and pelvic girdle. The chapter concludes with information on LSS in children and its role in palliative care.

INTRODUCTION

Until the 1970s amputation was the treatment of choice for primary high-grade malignant bone and soft-tissue tumors of limbs. The management of these lesions has changed dramatically since that time. Today about 85% of these patients undergo LSS. Instead of amputating part or all of the limb, the surgical team reconstructs the bony and soft-tissue defects using custom or modular endoprostheses, allografts, autografts, or composite materials.^{1,2} The procedure is performed in conjunction with chemotherapy and/or radiation therapy (neoadjuvant and/or adjuvant).^{1,2} Although LSS can enhance the quality of life it does cause a variety of functional impairments, and creates a need for early intensive rehabilitative intervention.^{1,2}

Rush² defined medical rehabilitation as "maximal preservation of physical, psychological, social, occupational, creative and economical function in conjunction to malignant disease and its treatment". It is a way to restore the patient's function to the highest possible level without considering the basic pathology.

For many years it has been assumed that investing in extensive rehabilitation efforts for patients with poor prognoses and short life expectancies could not be justified from an economic perspective.³ Now that cure rates among patients who have undergone LSS are 60–80%, this assumption is clearly no longer correct.³ It is no less important to rehabilitate patients with metastatic bone disease. Patients with pathological fractures or pending fractures are currently treated aggressively with internal fixation techniques that permit immediate weightbearing and full functionality. The goal is to avoid pain and maximize mobility for the remainder of the patient's lifetime, regardless of its length.⁴ The implication is clear: rehabilitation must become an integral part of the team approach to LSS.

This chapter describes the rehabilitation of patients who have undergone LSS. Because most of the authors' experience is with the use of endoprostheses, different aspects of this type of reconstruction are stressed.

LSS VERSUS AMPUTATION SURGERY

LSS can result in survival rates and disease-free periods that equal those achieved with amputation.² The presumed functional and psychological advantages of LSS over amputation, however, have yet to be established. LSS appears to offer the possibility of better psychological functioning and an intact body image, but it is more complex and demanding than amputation and is associated with more morbidity. The duration of surgery is longer, and infection, pain, and other postoperative complications are more common.^{1,5–7}

Otis *et al.*⁸ compared energy cost during gait in osteosarcoma patients after resection of the distal femur and knee joint and replacement with an endoprosthesis with that of patients who had undergone an above-knee amputation. The former had a lower energy cost during gait than the latter. Eiser *et al.*⁶ noted that one of the disadvantages of LSS is that additional hospitalizations may be necessary in the case of complications such as infections or loosening of the endoprosthesis. In children, repeat procedures are necessary for elongation of an extendable prosthesis.

It is important to emphasize that, in order to justify LSS, the procedure must provide limb function equal or superior to that provided by an external prosthesis after amputation. At the same time the tumor must be resected according to principles of oncologic surgery (i.e. there must be free margins and minimal damage to major neurovascular bundles and muscles). Despite the disadvantages, nearly all patients believe that an attempt to salvage a limb is worth the time and effort.⁵

PROBLEMS ASSOCIATED WITH LSS

LSS is an extensive procedure involving huge masses of soft tissues, bones, and joints, and resulting in long and deep scars. In contrast to ordinary general orthopedic procedures, in which the goal is to solve a local problem with minimal exposure of and damage to surrounding anatomic structures, LSS deliberately damages many anatomic areas and may cause the following problems.

Bone and Joint Damage

- Resection of bone with no replacement: in non-weightbearing (NWB) areas such as pelvic girdle, or dispensable bones such as the fibula, clavicle, or scapula. There is no need to replace or reconstruct them.
- Resection of bone and joint with replacement: this means the need for using endoprostheses (customized or modular), improvised internal implants/fillers such as nails, plates, and cement; allografts, and composites/combinations of the above.

Muscle Damage

- Resection of part of a muscle or group of muscles because of tumor involvement.
- Damage to muscle innervation because the nerve was involved in the tumor or had to be mobilized for tumor excision.
- Local transfer of muscles in order to cover implants or free microvascularized flaps.

Skin Damage

- Resection of skin areas involved by tumor, previous biopsy scars, or scars of other surgical procedures (in cases of local recurrence).
- Extensive use of skin grafts taken from other body parts.

Nerve Damage

- Excision of a nerve that is involved by tumor.
- Neuropraxia as a result of the need to mobilize major nerves during LSS.
- Local pressure on nerves during long surgical procedures.
- Direct nerve damage resulting from nonsurgical treatments such as radiotherapy and effects of neurotoxic agents.

Vascular Damage

- Excision of major vessels because of tumor involvement.
- Vascular damage during surgical exploration.
- Vascular spasm due to extensive mobilization of the bundle.
- Limb edema due to venous system damage.

Damage to the Lymphatic System

- Chronic swelling due to the long, deep, and extensive surgical exposures and scarring.

Scars

- Pain, dysesthesias, restricted range of movement (ROM) of joints, active muscle contractions, and blockage of lymphatic drainage can be caused by scars.

Infections

- Infections of bones, implants, and soft tissues are common because of the large areas exposed, the use of large implants, and the fact that many patients are immunocompromised as a result of radiotherapy.

Oncological Treatments

- *Radiotherapy* damages the skin, subcutaneous tissues, and muscles and causes fibrosis, decreased tissue elasticity, and contractures, resulting in joint stiffness. The consequence is delayed wound healing and limb edema. Osteonecrosis or osteopenia causes fragility and risk of fractures that do not heal.

- *Chemotherapy* causes chronic weakness and fatigue; it requires repeated hospitalizations, which make it difficult to maintain the intensity and continuity of a rehabilitation program.

The effects of ILP with TNF on the limb tissues are similar to those of radiotherapy. Although they are more acute, they are also more easily reversible.

THE REHABILITATION PROCESS

Rehabilitation of LSS patients is performed by a multidisciplinary team that includes an orthopedic oncologist, nurses, social workers, dietitians, physiotherapists, occupational therapists, and orthopedic technicians. To plan the pre- and postoperative management the team must understand the surgical procedure and its implications.

Steps in the rehabilitation process include a preoperative physical evaluation of limb function and disability, and pretraining the patient to reduce the rehabilitation time and emotional stress following surgery.

From the time the patient can leave his or her hospital bed to discharge home, the goal is to bring the patient as close as possible to independence in everyday life. Unlike many postsurgical patients, individuals who undergo LSS are not transferred to rehabilitation centers; instead they must return as soon as possible to chemotherapy or radiation therapy. Therefore, it is essential to distribute information about the surgery to the appropriate supporting medical teams in the community while closely following these patients for extended periods (see the Appendix).

TREATMENT TECHNIQUES AND ACCESSORY AIDS

The following techniques are useful at different stages of the rehabilitation process.

- *Improving ROM.* This is done manually by the therapist and with slings, continuous passive motion (CPM), and pulleys.
- *Muscle contraction.* This entails static contractions by manual actions. In advanced stages, open-chain exercises against gravity, springs, and weights are used, as are closed-chain exercises with weight lifting.
- *Pain-relief techniques.* These include electrotherapy, heat, massage, hydrotherapy, joint movements, and mobilization.
- *Soft-tissue treatment.* Surgery and radiation therapy damage tensile strength (TS) which is the ability of the tissue to stretch. The goal of treatment after soft-tissue injury is to encourage the tissue to regain its tensile strength as soon as possible.

The treatment principles are altered according to the healing stage of the tissue. There are four stages: injury, inflammation, regeneration, and remodeling. In the inflammation stage, for example, manual techniques are avoided because they influence the arrangement of the collagen fibers and there is a risk of breaking the fibrin network.⁹

Therapeutic Techniques

- Passive physiological stretching. This involves applying a longitudinal stretch to the tissue by using passive physiological joint movement.

Mobilization of Specific Soft Tissues

Scar Treatment

LSS leaves long and deep scars that cause adhesions of the skin and soft tissues. This limits ROM and causes pain. Mobilization of the scar is very important. Methods include deep friction and stretching, which make the scar soft and flexible. Ultrasound can be used to soften the scar.

Lymph Drainage

The lymphatic system is a fine drainage network that returns proteins and fluids into the circulation. It functions in only one direction. It begins in the intracellular space and gradually joins vessels that pass through the lymph nodes, finally draining into the main veins. Edema develops when fluids (rich in protein and fat) collect in the intracellular space after damage to the lymphatic system. Surgical wounds, especially deep ones, damage the lymphatic system. In addition, the deep scars of LSS impede lymphatic drainage.

The goal of lymph drainage is to reduce edema by influencing the superficial lymphatic network. This is done by applying fine and accurate manual movements in a certain pressure that activate the lymphatic system and produce a pumping action in the tissue.

Treatment also includes the use of special pressure bandages that help to maintain skin elasticity and prevent additional fluid congestion.

The pressure bandage is the main modality used to soften edema. Treatment should not be introduced until about 6 weeks after surgery, when the wound has healed and the patient's status is clear. Treatment should not be given during radiation therapy.¹⁰ In advanced stages of the treatment it is possible to use a Jobst pressure bandage (Jobst Ireland Ltd, Tipperary, Ireland). An accurate measurement is made to adjust a sleeve to the extremity.

Hydrotherapy

After completion of chemotherapy or radiation therapy, and considering the condition of the immune system, the skin, and the wound, it is possible to treat the patient with hydrotherapy. The buoyancy effect and relative lack of gravity, as well as the analgesic influence of warm water, allow easy performance of physical therapy requirements. On the other hand, water resistance can be used as a means of reinforcement of muscle strength.

Orthoses and Splints

Upper extremity orthoses are indicated when the extremity needs a mechanical support to prevent a fracture; there is a need to stabilize a joint in a functional position in order to prevent movement; or there is a neurological impairment.

Orthoses may be static or dynamic:

- *Static orthoses* include the cock-up splint, used for keeping a functional wrist position.
- *Dynamic orthoses* include a device used for radial palsy.

Lower extremity orthoses include the static *peroneal splint*, which keeps the dorsiflexion in 90° after damage to the peroneal nerve, and the *foot positioner*, which resembles a peroneal splint.

REHABILITATION CONSIDERATIONS OF SPECIFIC ANATOMIC SITES

Distal Femur and Knee Joint

The distal femur is the most common location for benign and malignant primary bone tumors. It is the site where the most experience has been gained with LSS.¹¹ The following details are relevant for the rehabilitation team:

1. The surgical approach depends on the tumor location (lateral or medial).
2. Extent of resection of the distal femoral bone (1/3, 1/2, or 2/3).
3. Resection of the muscle ends: vastus intermedius muscle (always resected), vastus medialis, vastus lateralis, rectus femoris, medial hamstrings (semitendinosus, semimembranosus), lateral hamstrings (biceps femoris), gracilis, sartorius, medial and lateral gastrocnemius muscles (the origin is always resected).
4. Replacement of the distal part of the femur by an endoprosthesis/allograft and stabilization of the stem (cemented/noncemented).
5. Replacement of the knee joint, including the tibial surface (usually not including the patella).

6. Type of endoprosthesis. Two types of endoprosthesis are used at the knee joint: a constrained (hinged) device, which enables movement in one plane (flexion/extension), and a semiconstrained (rotating hinge) device, which enables movements in two planes (rotation and flexion/extension). The rotating hinge provides varus–valgus and anteroposterior stability but allows rotation between the femur and the tibia. The constrained joint is more stable and is widely used in patients with large resections or in patients with a poor prognosis.
7. Local muscle flap transfer to cover the endoprosthesis (transferring the gastrocnemius muscle anteriorly to cover the endoprosthesis) or transferring the muscle to reinforce the loss of major quadriceps mass (suturing the hamstrings anteriorly).
8. Nerve impairment: peroneal nerve palsy (in the lateral approach) is quite rare; femoral nerve and tibialis posterior nerve impairment are rare.
9. Leg-length discrepancy: up to a 2 cm shoe insert can be given; when more is required it is necessary to raise the shoe.

Principles of Rehabilitation

1. A knee immobilizer is used for 3–6 weeks or until the soft tissues are satisfactorily healed and the quadriceps muscle is strong enough to stabilize the knee while walking.
2. ROM: knee flexion with CPM (**Figure 36.1**) is started 5–7 days after surgery, if the wound is healed. Afterwards, the patient starts performing assisted

active and active flexion exercises. The range of extension should be monitored by the therapist.

3. Muscle strengthening: extension (quadriceps) and flexion (hamstrings, gastrocnemius) are supported by static contraction, assisted active, and active exercises (e.g. open- and closed-chain exercises).

While the degree of quadriceps resection is an important factor influencing the knee extension strength and the functional outcome, it is not the only one. Other factors are history of deformity, details of the surgical technique leading to changes in muscle fiber orientation and length–tension properties, postoperative perioperative scar tissue, prosthetic design, and the rehabilitation program.^{12,13}

4. Ambulation: the goals in terms of activities of daily living include: independence in transfers (e.g. bed to chair) and, in cases of peroneal palsy, the use of a peroneal splint, in order to facilitate correct stepping. In cases where a cemented endoprosthesis is used, walking with weightbearing using crutches is permitted and, if the custom prosthesis is not cemented, weightbearing should be deferred for at least 6 weeks.

Complications

Patellar dislocation is rare and observed only after resection of the vastus lateralis.¹¹

PROXIMAL TIBIA AND KNEE JOINT

This is the second most common site for primary benign and malignant bone tumors. LSS in this site is more difficult than in most other anatomic sites because of the lack of soft-tissue covering.¹⁴ The following details are relevant for the rehabilitation team:

1. The surgical approach depends on the tumor location (lateral or medial).
2. Extent of resection of the proximal tibial bone (1/3, 1/2, 2/3).
3. Extent of resection of the proximal part of the fibula (tibiofibular joint only, fibular head, or proximal third of the fibula).
4. Detachment or complete resection of the patellar tendon.
5. Surgical options for reconstruction of the extensor mechanism: (a) suturing the patellar tendon to the hook on the endoprosthesis with Dacron tape; or (b) suturing the gastrocnemius muscle above and to the patellar tendon stump to reinforce the extensor mechanism. The transposing of the medial gastrocnemius muscle, lateral gastrocnemius muscle, or both, with a skin graft is used also to cover the endoprosthesis.



Figure 36.1 A CPM machine is utilized following distal femoral replacement only if the wound is well healed. In general this does not begin until postoperative day 5–7.

6. Detached muscles: biceps femoris muscle, pes anserinus muscles and the popliteus muscle (always resected).
7. Detachment and transfer of muscles to cover the endoprosthesis: medial/lateral gastrocnemius muscles.
8. Partial muscle resection: all the attached muscles to the resected proximal tibia (anterior tibialis, extensor digitorum longus, extensor hallucis, soleus, flexor digitorum longus).
9. Replacement of the proximal part of the tibia by an endoprosthesis and stabilization of the stem (cemented/noncemented).
10. Replacement of the knee joint. This procedure resembles that used for the distal femur. In addition, there is a hook on the tibial body that is used for attachment of the reconstructed patellar tendon (pseudotibial tuberosity).
11. Peroneal palsy (deep and/or superficial peroneal nerve) is more common in these operations because of the proximity of the nerve to the operating area or the tumor itself.
12. Leg-length discrepancy (same as the distal femur).

Principles of the Rehabilitation Program

The knee is kept in extension using a brace for 4–6 weeks to permit healing of the new joint capsule and the patellar tendon, and to enable the establishment of a good extensor mechanism.¹⁴

1. Muscle strengthening: during this period, which lasts from 4 to 6 weeks, the patient strengthens the knee muscles and the extremity muscles. Static, assisted active, active, and weightbearing exercises are used.
2. ROM: after removal of the brace the patient starts gradually flexing the knee using CPM and active exercises.
3. Ambulation: partial weightbearing with a walker or crutches is used for the first 4–6 weeks and full weightbearing is used thereafter. A peroneal splint is used in patients with peroneal palsy.

Complications

These patients experience varying degrees of extension lag and late extensor mechanism rupture.¹⁴ There are several ways to reconstruct the extensor mechanism:

1. Gore-Tex reinforcement: using the middle third of the quadriceps muscle tendon, together with part of the patellar surface, and creating a "new" patellar tendon reinforced with Gore-Tex (W.L. Gore and Associates, Inc., Flagstaff, Arizona, USA) implants.¹⁵
2. Fibula transposition: the proximal fibula is ventralized and medialized, and the patellar ligament is sutured

to the stumps of the tendon of the biceps femoris muscle and the lateral collateral ligament on the fibular head.¹⁶

3. Transposition of the gastrocnemius muscle: reconstruction is accomplished using a strap of fascia and transferring the femoral insertion of one or both heads of the gastrocnemius muscle.¹⁶
4. A combination of the above.¹⁶

PROXIMAL HUMERUS AND GLENOHUMERAL JOINT

The shoulder girdle consists of the proximal humerus, scapula and clavicle as well as the surrounding muscles. The proximal humerus and the scapula are the third most common sites of primary bone sarcomas. Tumors at this site are likely to involve the deltoid muscle and the axillary nerve, and they are almost always sacrificed when the proximal humerus is resected. In most cases shoulder function is severely damaged but extremity function is close to normal.¹⁷ From a rehabilitation perspective, LSS in the shoulder offers a superior functional outcome to forequarter amputation or shoulder disarticulation.¹ The following details are relevant for the rehabilitation team:

1. Extent of resection of the proximal humerus (1/3, 1/2, 2/3).
2. In many cases resection of the lateral part of the clavicle and parts of the scapula (the acromion, coracoid process, glenoid fossa, or all of these).
3. Detachment and/or resection of muscles: the deltoid muscle and the long head of the biceps brachii muscle are almost always resected. Insertions of the three muscles of the coracoid process, rotator cuff, pectoralis major and minor, teres major, latissimus dorsi, triceps brachii, and trapezius muscles are almost always excised.
4. Replacement of the proximal humerus with an endoprosthesis and stabilization with a cemented/noncemented stem.
5. Creating a concave surface on the lateral border of the scapula as a pseudoglenoid when needed.
6. Suturing the remaining muscle stumps to each other and to the endoprosthesis (pseudo greater tuberosity).
7. Nerve resection (mostly the axillary nerve).

Principles of the Rehabilitation Program

For the first 3–4 days the hand is stabilized to the body (bulky, Dessaut-like dressing). At this stage the patient moves the elbow, wrist, and hand. After the bulky dressing is removed only a pendular movement in the

"shoulder joint" is permitted for 3–4 weeks. Active and passive movements in the scapula (elevation, depression, protraction, retraction) are permissible. As a result of the surgical procedure (i.e. muscle detachment, lack of joint stability, weight of the extremity with the endoprosthesis, pain), the patient's ability to posture the head, neck and the shoulder girdle is impaired. It is important to instruct the patient on proper posture, after which passive and assisted active exercises are initiated.

The active exercises should be focused on enhancing the patient's functional ability. Occupational therapy has a very important role in training the limb to be a usable "helping hand". During rehabilitation it may be necessary to use accessory aids: a simple *sling* in the first stages to help overcome the weight of the limb, a *band* that holds the limb adducted to the body so that the limb will stay attached while the patient changes position in bed, and a *shoulder mold* that improves the contour of the cosmetic deformity in the shoulder caused by the lack of muscle tissue.

PROXIMAL FEMUR AND HIP JOINT

The proximal femur is the fourth most common location for primary bone sarcomas. Most tumors of the proximal femur can be managed by LSS. The femoral vessels, femoral nerve and sciatic nerve are rarely involved by tumor. Rehabilitation may take up to 1 year.¹⁸ The following details are relevant for the rehabilitation team:

1. The surgical approach is almost always lateral (anterolateral or posterolateral shift).
2. Extent of the proximal femur (1/3, 1/2, etc.).
3. Resection of all the muscle insertions that are attached to the proximal femur (i.e. iliopsoas, external rotators, gluteus medius/minimus, and (sometimes) part of the gluteus maximus, adductors, and quadriceps muscles). The tensor fascia lata muscle and the iliotibial band (ITB) are almost always damaged during the surgery.
4. Replacement of the proximal femur with an endoprosthesis/allograft (cemented/noncemented). A bipolar cup is used whenever possible. This is better than total hip arthroplasty because it gives greater stability and has less risk of dislocation.¹⁸
5. Suturing most of the muscle stumps to each other in order to cover the implant and create a pseudocapsule that will protect the implant from dislocations and infection.
6. Attachment of the abductors into a hook on the endoprosthesis (pseudo greater trochanter).
7. Leg-length discrepancy.

Principles of the Rehabilitation Program

1. For 6–8 weeks the patient should avoid adduction, flexion over 90°, and internal rotation about the hip joint.
2. The leg has a tendency to fall into external rotation because the adductors and the external rotators of the hip are "attached" in a shorter position during the surgical procedure. The leg should be kept in a neutral position within a splint (see Figure 36.2).
3. Exercises to improve ROM of the hip and knee joints.
4. Muscle strengthening: gradually exercising to improve active mobility of the hip joint and strengthening the muscles without gravity is recommended for the first 4–6 weeks (within the limits of pain). The gluteus medius and tensor fascia lata muscles are attached to the ITB. The surgical wound damages the ITB and causes a scar, which shortens the band; therefore the hip tends to be in abduction. The gluteus medius is in its inner range, which leads to weakness. As a result it is important to strengthen the gluteus medius and stretch the ITB.¹⁹
5. Ambulation: the patient walks with a walker or crutches for 6–12 weeks, then switches to a cane. Except for the elderly, most patients are eventually free from ambulatory aids. Some have a Trendelenburg gait because of weakened abductors.



Figure 36.2 Following a distal femur or proximal tibial replacement there is a normal tendency for the knee component to rotate externally due to gravity until the muscles are strong enough to maintain the leg in a neutral position. Therefore, an external foot splint is utilized as shown.

Complications

Hip dislocation and a Trendelenburg gait.

PELVIC GIRDLE

The pelvic anatomy is complex, and resection and reconstruction of bony tumors and defects in this area are more difficult than LSS of cylindrical long bones. The pelvis is covered by a large mass of muscles that usually restrict the tumor from reaching the adjacent vessels and nerves; however, there is occasional damage of the nerves (sciatic or femoral).²⁰ Moreover, involvement of internal organs in the pelvic space (uterus, bladder, bowel) may require excision or reconstruction.

There are four types of pelvic resection:²⁰

Type I – ilium: usually includes resection of the gluteus medius, gluteus minimus, and iliacus muscles. The sartorius, tensor fascia lata and abdominal muscles are detached.

Type II – periacetabulum: the major muscle detached is the rectus femoris.

Type III – ischium and pubis: the detached muscles include the hamstrings, external rotators, adductors, and gracilis.

Type IV – perisacroiliac joint: the major detached muscle is the gluteus maximus.

Types of reconstruction include: (a) various improvisations using nails, plates and cement, and bone graft; (b) saddle prosthesis – fixed distally to the femoral diaphysis (the head and neck of femur are resected) and proximally hinged under the remaining ilium; (c) custom-made implants or allografts, and (d) arthrodesis. Not all pelvis resections require reconstruction.

Principles of the Rehabilitation Program

1. The patient remains in bed for 4–7 days, depending upon the extent of surgery.
2. The patient is taught to mobilize in bed (e.g. use of the other limb, the torso).
3. When getting out of bed the patient starts partial weightbearing (PWB) with ambulatory aids.
4. Occasionally there is a need to teach some special techniques and to use aids to help in ambulation (e.g. hiking of the nonoperated side to help in moving the operated leg, raising the shoe of the nonoperated leg).
5. General strengthening of the muscles of the lower extremities.

Complications

These include a Trendelenburg gait, dislocations, and fractures around the hip or pseudohip, surgical

damage to the sciatic or femoral nerve, and visceral injuries (e.g. to the bladder, rectum).

LSS IN CHILDREN

The most common primary malignant bone tumors in children are osteosarcoma and Ewing's sarcoma. They develop in the same anatomic locations as in adults, namely the knee and shoulder joint areas.

Children who undergo LSS, in contrast to adults, need to be hospitalized repeatedly for lengthening procedures. This prolongs rehabilitation and causes repeated cycles of functional regression because of soft-tissue stretching and stiffening that follow each procedure.

During LSS the operated leg is lengthened by up to 2 cm if possible. When the adjuvant chemotherapy and/or radiation therapy has ended, and the child has grown, the procedures for lengthening the extremity begin. Each lengthening operation extends the extremity between 1.5 and 2 cm. The procedure is carried out once or twice a year, according to the individual rate of growth. Once the skeleton reaches maturity the endoprosthesis is changed to its final form.

In children, endoprostheses are usually noncemented. As a result of the repeated lengthening procedures, various complications may develop. These include higher rates of infections, thick scarring that limits ROM of the adjacent joint, stiffness of soft tissue because of the repeated stretching, higher chances for vascular and nerve damage, skin problems, lack of muscular cover, and a frequent need to lengthen tendons.

After each lengthening procedure the child needs to return to the rehabilitation program and learn to cope again and again with the above problems.

Principles of Rehabilitation

The aims of rehabilitation include enhancement of ROM of joints, muscle strengthening, scar treatment, soft-tissue mobilization, and provision of ambulatory aids (e.g. crutches) if needed.

Many children experience psychological problems during the course of the disease. Frequent hospitalizations for surgery, chemotherapy, or radiotherapy necessitate lengthy absences from school. Young children feel frustrated by being isolated from their environment. "There is a loss of opportunity for play, feelings of inadequacy due to impaired mobility, problems at school and fears of separation and death" according to Frieden *et al.*⁵ The child might feel victimized. Depression or bad moods can influence the

rehabilitation process and the child's ability to cope. The issues affecting teenagers are often related to their body image. They may have difficulties coping with disfigurement and physical disability. In addition, there are problems in identifying with their peer group and concern as to how patients are perceived by members of the opposite sex. Their families might experience guilt or be overprotective.

It is the therapist's duty to deal with all these problems, acquire the child's trust, bond with the family, and accompany the patient and family throughout this period.

REHABILITATION IN PALLIATIVE ONCOLOGY

Rashleigh⁴ described palliative care as having a holistic focus; that is, it refers to the active interdisciplinary care, including an effort to meet the physical, social, psychological, and spiritual needs of the patient and his or her family or caregivers.⁴ Many cancers metastasize to bone (spine, pelvis, ribs, and long bones). Metastases weaken the bones and increase the risk of pathological fractures. The patients are operated upon for pending fractures, fractures, and intractable pain.⁴ The aims of palliative treatment are to control pain, increase mobility, reduce dependence, and enhance the quality

of life. The complex issue of physical palliation of the terminally ill involves aspects of musculoskeletal, neural, respiratory and circulatory therapeutic management, as well as education.⁴

The components of rehabilitation treatment in the palliative setting include:

1. Mobilization and ambulation prevent the patient from becoming bedridden and developing bedsores, osteopenia, hypercalcemia, and respiratory and urinary tract infections.⁴
2. Pain relief by electrotherapy (TENS), hydrotherapy, and medications, including opiates.
3. Respiratory therapy.
4. Accessory aids and modification of the patient's surroundings.

An essential element of a home visit assessment is the education of palliative care patients and their caregivers to utilize energy conservation strategies and employ mechanical aids to cope with limited physical resources.⁴

Despite the short period of time that the patient will survive, intensive rehabilitation can improve the quality of life, enable the patient to return to his or her familiar surroundings, bring optimal independence of function, and help avoid dependence.^{4,21}

APPENDIX: RESECTION OF THE DISTAL FEMUR AND KNEE JOINT (A SAMPLE PROTOCOL FOR THE COMMUNITY REHABILITATION TEAM)

Surgical Procedure

- Surgical approach (lateral/medial)
- Resection of the distal femoral bone (1/3, 1/2, or 2/3)
- Resection of muscle ends: vastus intermedius, vastus medialis, vastus lateralis, rectus femoris, medial hamstrings, lateral hamstrings, gracilis, sartorius, medial and lateral gastrocnemius.
- Replacement by an endoprosthesis/allograft/auto-graft composite. Stabilization of the stem (cemented/noncemented)
- Replacement of the knee joint (constrained/rotating hinge)
- Muscle flap transfer: _____
- Nerve impairment (Yes/No)? Which? _____
- Leg-length discrepancy: _____ cm
- Comments

Hospitalization

Days 1–5 after surgery

- Resting cast/splint for 3 days
- Quadriceps muscle – static contraction

- Out of bed to the armchair: 2–3 days after surgery
- After cast removal: exercises to improve flexion and ROM using CPM
- Passive movement of the ankle in cases of peroneal palsy

5 days after surgery until discharge from hospital

- Walking PWB/NWB with walker/crutches for 6 weeks
- Knee immobilizer
- Exercises: climbing stairs
- Peroneal splint as needed
- Raising of shoe as needed
- Knee muscle strengthening: start with assisted active exercises in supine, prone, and sitting positions (using slings, pullies, or springs without weightlifting for the first few weeks)
- Electrotherapy if needed
- Ankle dorsiflexion when needed
- Patient's condition at time of discharge:

After discharge (± 2 –6 weeks)

- Ambulation: gradual exercise to improve weight-bearing; stop use of the accessory aids, including the knee mobilizer
- Continuation of muscle strengthening: add closed-chain exercises (while standing) to strengthen the quadriceps muscle, stair climbing, exercises to improve weightbearing
- Treatment of the scar after removal of the sutures

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Appendix A: Abdominoinguinal Incision for the Resection of Pelvic Tumors

Constantine Karakousis

OVERVIEW

The abdominoinguinal incision allows a vast improvement in the exposure and resectability of tumors in the lower abdomen with fixation to the pelvic side wall. A midline abdominal incision is connected to a longitudinal inguinal incision across the inguinal ligament. The pelvic side wall is directly exposed by detachment of the rectus muscle from its origin on the pubic crest and by division of the inguinal canal along the spermatic cord. This exposure allows safe resections along the iliac vessels without tumor spillage. The abdominoinguinal incision should be part of the armamentarium of every surgeon willing to accept responsibility for pelvic and pelvic side wall malignancy.

INTRODUCTION

Pelvic tumors with lateral fixation present difficulties in their resection, primarily due to inadequate exposure through conventional abdominal incisions. The difficulty arises especially with tumors in the lower parts of the pelvis where the anterior abdominal wall converges with the retroperitoneal structures (e.g. iliopsoas muscle, iliac vessels). In this area the inguinal ligament spanning between the anterior superior iliac spine and the pubic tubercle provides an obstacle to unhindered exposure.

A midline, paramedian, or oblique abdominal incision often does not provide adequate exposure for these tumors. These incisions render sufficient exposure for the dissection and control of the common iliac vessels proximally, below the bifurcation of the aorta, but do not afford exposure of the terminal portion of the external iliac vessels because the presence of tumor hinders further visibility. Often these tumors are considered unresectable or are managed with hemipelvectomy.

Queral and Elias reported a two-stage procedure for removal of a sarcoma localized in the right iliac fossa with involvement of the iliac vessels.¹ In the first operation a femorofemoral bypass was performed from the left side to the right, and the common femoral artery was proximally ligated and divided. In the second operation, through an abdominal incision the mass was resected with en-bloc resection of a segment of the right iliac vessels, which were ligated and divided proximally. This example provides a solution to the distal control of the iliac vessels, but it requires two operations, and exposure at the time of resection of the tumor mass through an abdominal incision remains suboptimal.

What is needed for the resection of these tumors is an incision that would simultaneously provide an continuity in exposure of the abdominal cavity and one or both groins so that both iliac and femoral vessels would

be exposed in one field. For this incision an abdominal component would be needed and an incontinuity inguinal component, i.e. an abdominoinguinal incision. The inguinal ligament would have to be divided to allow uninterrupted exposure and control of the iliofemoral vessels.

A lower midline incision provides good exposure of the intrapelvic structures. An inguinal incision exposes the femoral vessels. A transverse incision connecting the two, by dividing the origin of the rectus abdominis from the pubic crest and the insertion of the inguinal ligament to the pubic tubercle, provides the necessary link that allows a single incontinuity field and optimizes exposure. Although in the preceding discussion we arrived at the abdominoinguinal incision deductively, in reality I stumbled upon variations of it in the first few cases in the process of designing an incision for a specific tumor.² Later I realized that this could be developed into a formal incision for exposure in the lower quadrants of the abdomen. The abdominoinguinal incision may function much in the same way that the thoracoabdominal incision is used for the upper quadrants of the abdomen.³

INDICATIONS

The indications for the abdominoinguinal incision are: (1) abdominal or pelvic tumors extending over the iliac vessels, (2) tumors in the iliac fossa ([Figure A1](#)), (3) primary tumors, possibly involving the iliac vessels or large iliac lymph node metastases, (4) tumors with fixation to the wall of the true pelvis or large obturator nodes, (5) tumors involving the pubic bone with or without extension to the pelvis or adductor group of muscles, and (6) tumors of the groin when they involve the vessels of the lower abdominal wall or extend in the retroperitoneal area.

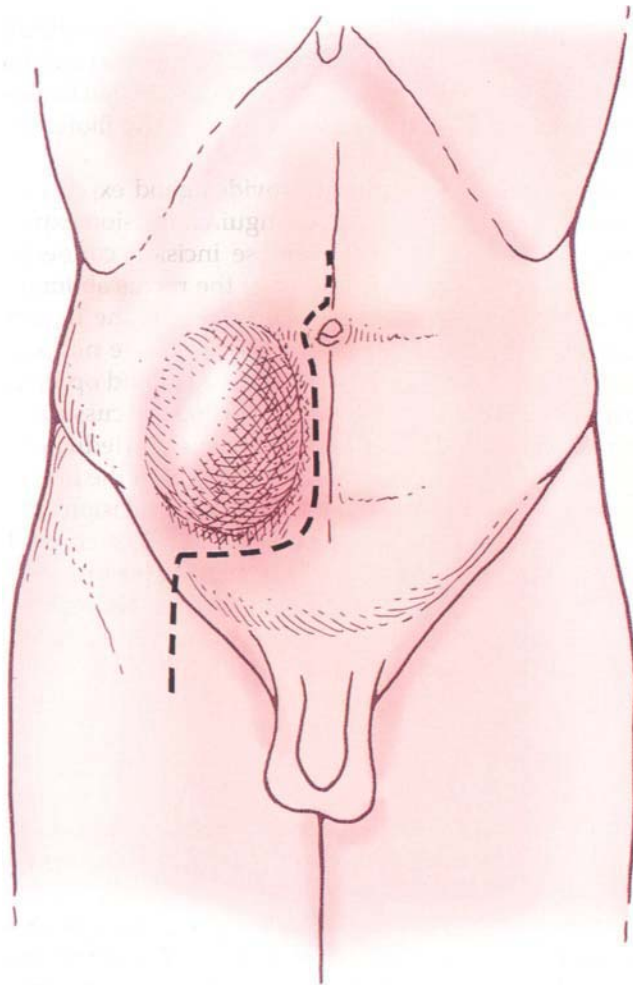


Figure A1 Position and incision. With the patient in the supine position, a lower midline abdominal incision is outlined from just above the umbilicus to the pubic symphysis. The peritoneal cavity is entered, and exploration is carried out to assess the extent of disease. Preliminary dissection between the tumor mass and midline pelvic structures may be carried out. Involvement of the latter does not necessarily mean unresectability, of course, since they can often be removed en-bloc with the tumor. When there is a question of involvement of the iliac vessels distally, the common iliac vessels are dissected free and vessel loops are passed around them.

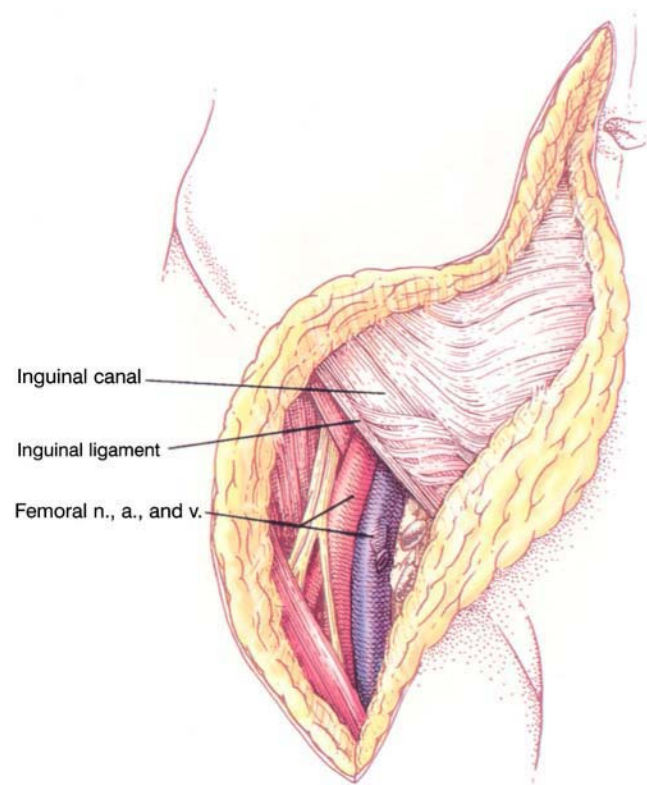


Figure A2 Incision through inguinal canal. If the decision is made to proceed with the resection the lower end of the incision is extended transversely to the midinguinal point and then vertically, over the course of the femoral vessels, for a few centimeters. The vertical portion of the incision is deepened to expose the common femoral vessels.

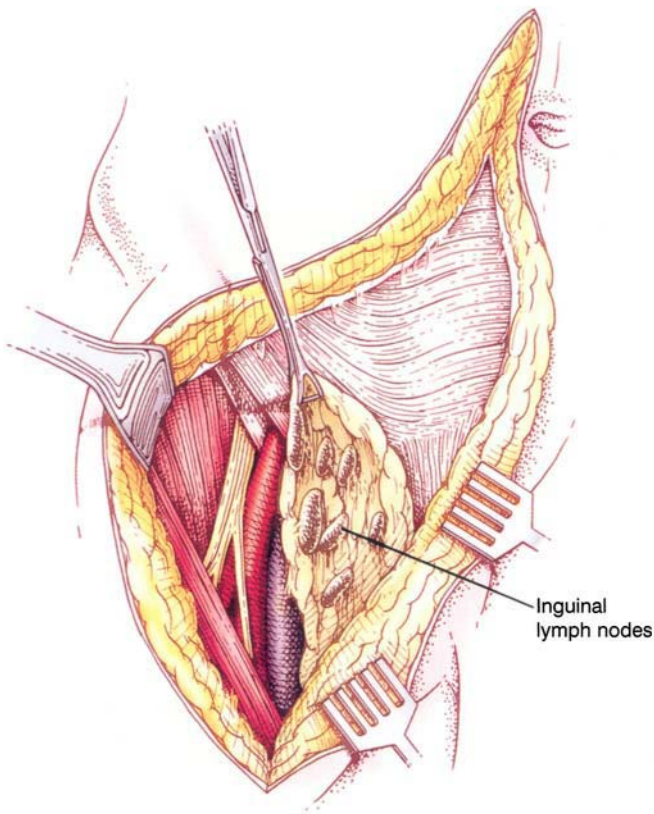


Figure A3 Dissection of inguinal nodes. When the operation is performed for large iliac and/or obturator nodes, or if there is clinical or potential microscopic involvement of the inguinal nodes, the vertical portion of the incision is made to extend to the apex of the femoral triangle, flaps are raised as in a groin dissection,⁴ and the nodes are mobilized off the femoral vessels, but their proximal continuity with the deep nodes is preserved.

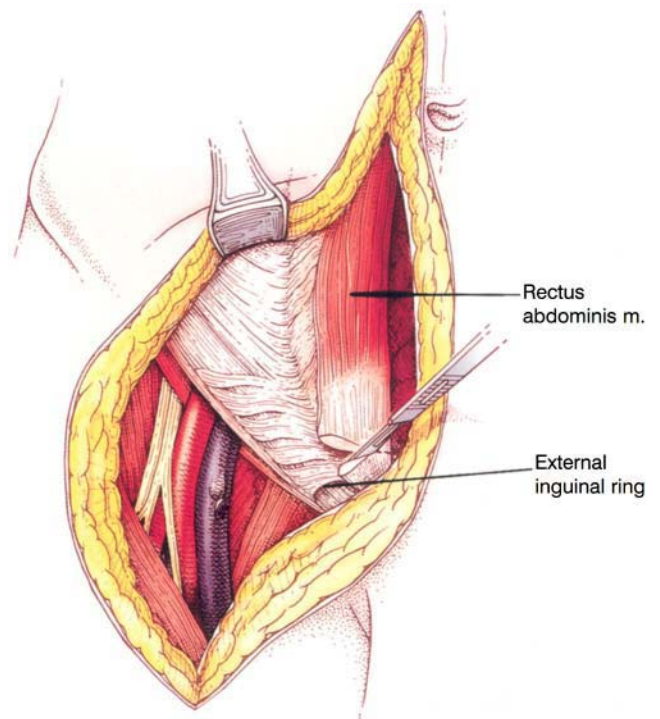
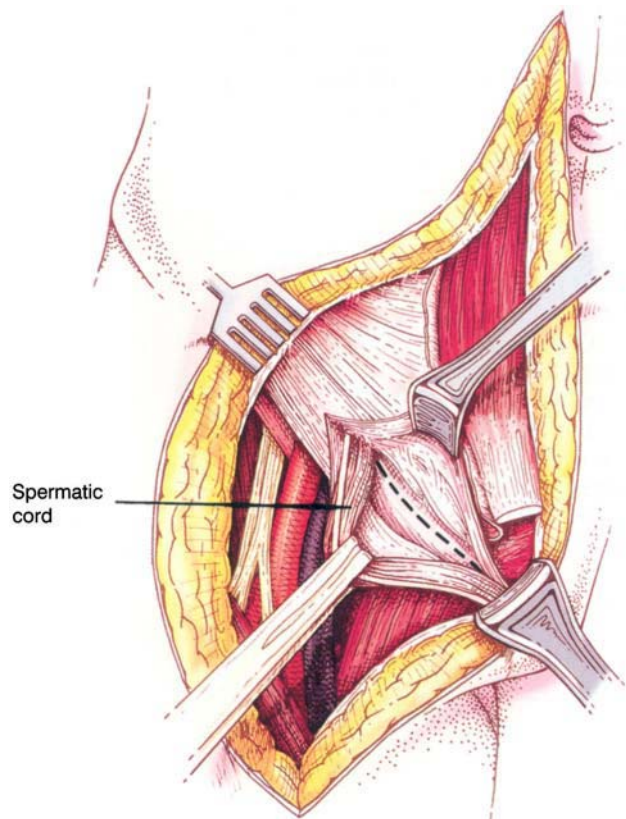


Figure A4 Division of rectus abdominis muscle. The transverse portion of the incision is deepened to the surface of the anterior rectus sheath, which is divided, and the rectus abdominis muscle is transected a few millimeters from its origin on the pubic crest. This incision is through its tendinous portion.

Figure A5 (right) Incising the floor of the inguinal canal. The inguinal canal floor is divided in the same direction up to and including the medial border of the internal inguinal ring. In so doing, the spermatic cord is displaced medially. Alternatively, after division of the medial crus the inguinal floor may be incised from inside and the cord exposed from within the abdomen and extracted from the inguinal canal for medial displacement. Deep to the internal inguinal ring the structures of the cord deviate, the vas deferens coursing medially, and the internal spermatic vessels toward a lateral and cephalad direction. Depending on the location of the tumor, the internal spermatic vessels may have to be divided at this level; this maneuver usually leaves a viable ipsilateral testis. Division of the cord at the level of the external inguinal ring does not require ipsilateral orchiectomy but will be accompanied by testicular atrophy.



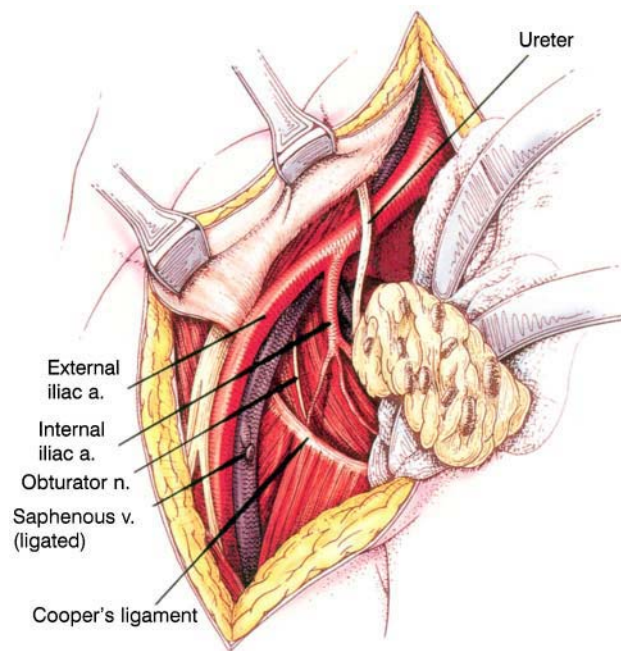


Figure A6 Exposure of the pelvic side wall. The inguinal ligament is then divided at the pubic tubercle and dissection carried on its undersurface until the inferior deep epigastric vein and artery are encountered, ligated, and divided. The lateral third of the inguinal ligament is then detached off the iliac fascia. This allows the completion of the abdominoinguinal incision and provides wide exposure of abdomen and pelvis.

Further dissection depends on the location of the tumor. If the tumor is simply a pelvic mass extending over and obscuring the iliac vessels, the improved exposure now makes easy the dissection of the mass off the vessels and safe ligation of any tumor feeding branches. For large nodes the dissection is carried on the surface of the iliac vessels which are skeletonized. For a tumor located in the iliac fossa, the femoral nerve is located lateral to the femoral artery, immediately posterior to the continuation of the iliac fascia. A vessel loop is passed around it. Further cautious dissection along this nerve determines its relation to the tumor and whether it can be saved. If the tumor involves the vessels, proximal and distal control are secured and the dissection completed around the tumor mass, with any involved organs removed en-bloc. When the specimen is held only by the attachment to the vessels, the patient is heparinized, vascular clamps are placed proximally and distally, the specimen is removed, and vascular reconstruction is performed.

When the iliofemoral vessels are to be resected, the profunda femoris branches may have to be divided at a distance from the tumor in order to allow the mobilization of the specimen.

For tumors attached to the wall of the lesser pelvis or the obturator fossa, the improved exposure usually allows their resection. For tumors involving the pubic bone, following the completion of the abdominoinguinal incision, the adductor muscles are divided off the pubic bone at an appropriate distance from the tumor and the anterior and posterior pubic rami are exposed: the former just medial to the acetabulum and the latter medial to the ischial tuberosity. With the help of a right-angle clamp a Gigli saw is passed around the pubic symphysis, which is divided along with the anterior and posterior pubic rami. The obturator nerve and vessels have to be divided proximally because they course through the obturator foramen. The defect may be replaced with a polypropylene mesh.

For a large tumor located in the groin, covering or involving the entire length of the common femoral vessels and possibly the lower abdominal wall, the abdominoinguinal incision provides continuity exposure of the iliofemoral vessels. In making the incision, flaps may have to be raised around the mass. If the lower abdominal wall and inguinal ligament are involved, following transection of the anterior rectus sheath and rectus abdominis muscle off the pubic crest, the incision is continued through the external oblique aponeurosis and internal oblique and transversus abdominis muscles at a sufficient distance from the tumor. The inguinal ligament is divided off the anterior superior iliac spine and the pubic tubercle, and thus the lower abdominal wall muscles and inguinal ligament are removed en-bloc with the tumor. The inferior epigastric vessels are divided at the point they proceed behind the rectus muscle.

In **Figure A6** the lateral third of the inguinal ligament has not been detached off the iliac fascia, a step providing further exposure.

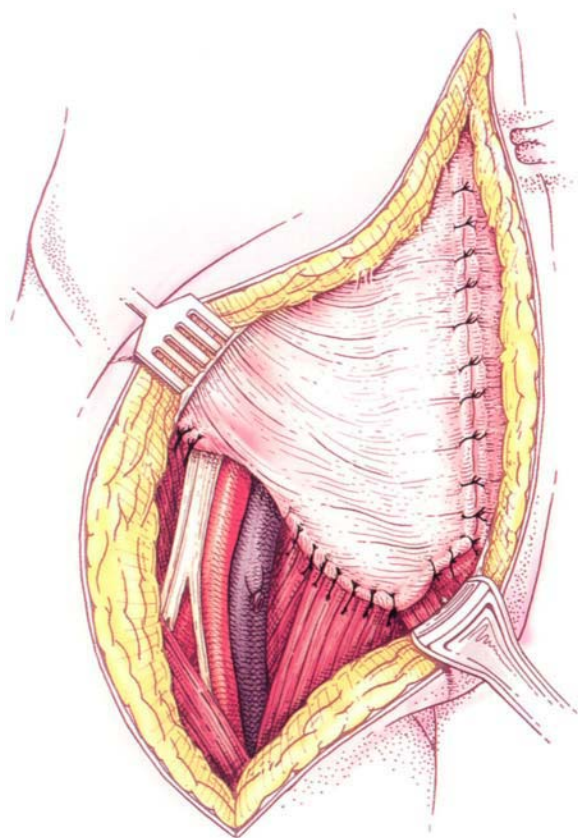


Figure A7 Deep closure. The closure of the abdominoinguinal incision is uncomplicated. Lateral to the vessels the inguinal ligament is approximated to the iliac fascia and medial to the vessels to Cooper's ligament. The rectus sheath and muscle are approximated to their remnants on the pubic crest. A suction drain is placed in the inguinal portion of the incision. A subcutaneous layer of absorbable material may be used. The skin and the midline portion of the incision are closed in a routine fashion. The sartorius muscle may be detached from its origin on the anterior iliac spine and rotated to provide a nice muscle coverage of the exposed femoral triangle vessels and nerves.

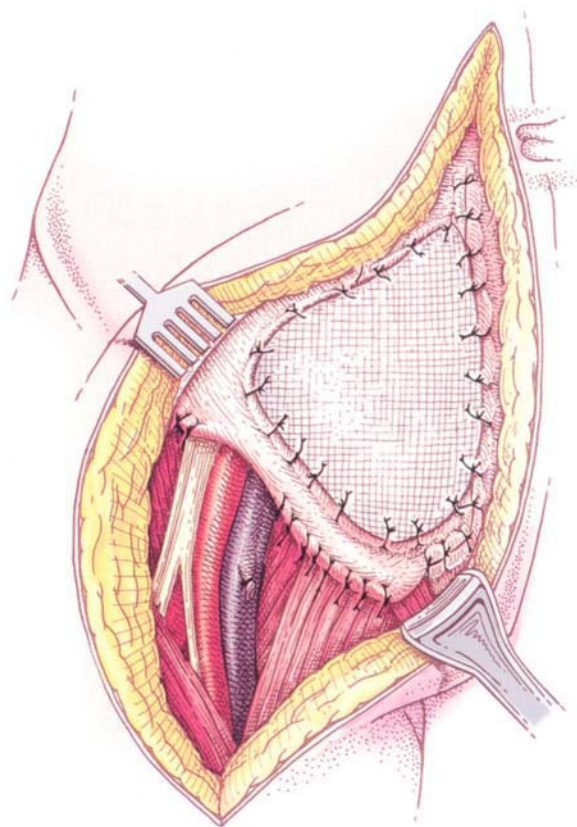


Figure A8 Deep closure requiring mesh. When a defect in the fascia has been created, it may be covered with a plastic mesh, which also replaces the inguinal ligament. The mesh should not be in direct contact with the vessels. This can usually be done by dividing the sartorius muscle distally at the apex of the femoral triangle and mobilizing the distal end so that the vessels are covered, taking care to avoid devascularization of this muscle.

When the defect in the groin also involves the skin, we have used the contralateral rectus abdominis muscle which is divided proximally and rotated with the posterior sheath attached to it, its blood supply deriving from the inferior epigastric vessels. The muscle is sutured to the defect and skingrafted immediately.

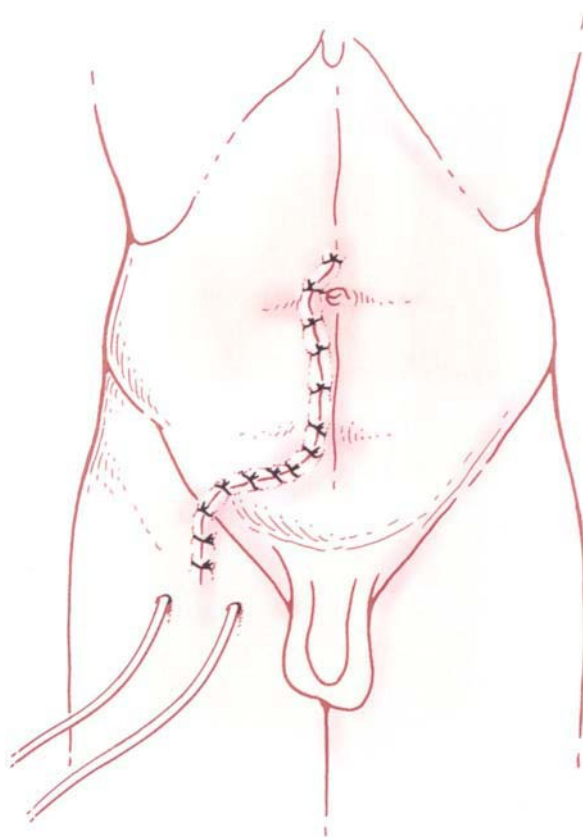


Figure A9 Skin closure.

DISCUSSION

The abdominoinguinal incision has been used in over 50 patients with a variety of tumors, usually soft-tissue sarcomas. One of these patients had adenocarcinoma of the sigmoid fixed to the iliac fascia. This tumor was thought to be unresectable at another hospital, but was successfully removed through this incision. The majority of the patients had been operated on once or twice elsewhere, and were found to be unresectable or thought to need a hemipelvectomy.

All these tumors, presenting with fixation to the soft tissues of the wall of the pelvis, were resected with the abdominoinguinal incision, with the exception of two patients. They required hemipelvectomy due to extensive nerve involvement. One patient required an abdominobiinguinal incision, i.e. bilateral extension of the abdominal inguinal midline incision to the groins. Tumors involving the innominate bone, with the exception of the medial portion of the pubic bone, are resected best with the use of the techniques of internal hemipelvectomy,⁴ and, if necessary, hemipelvectomy.

The abdominoinguinal incision heals well without complications. In the event of a previous transverse incision in the lower quadrant, which may have interrupted the connection to the superior epigastric vessels and the distal portion of intercostal and lumbar branches, a small area of necrosis at the junction of the midline and transverse portions of the incision may occur, since this incision divides the inferior epigastric vessels. In two patients with this condition a small area of ischemic necrosis developed, which, following debridement, healed by secondary intention.

There was one death 2 weeks postoperatively, which resulted from erosion and hemorrhage of a previously heavily radiated external iliac artery that was in contact with a mesh used to replace a fascial defect. It is important therefore to cover the vessels with the sartorius or rectus femoris muscle (by dividing its origin from the anterior inferior iliac spine and displacing it medially) when a mesh is placed adjacent to the vessels or when there is concern about pap necrosis. No instances of postoperative incisional hernia have been noted.

The abdominoinguinal incision renders resectable the majority of pelvic tumors with lateral fixation to the soft tissues of the pelvis and, through improvement in exposure, allows for a safe, deliberate dissection. It is the counterpart of the thoracoabdominal incision for the upper quadrants of the abdomen. The results from the use of this incision obviously depend on the histologic type and stage of the tumor and the expected margin of resection one can thus obtain. It should be used when appropriate and in the context of the biology of the tumor, the expected margin, and the possible use of adjuvant treatments.

In many situations in which the tumor is not laterally fixed, but when it is large and distal and pressing against the obturator foramen(s) or the obturator areas, one can obtain sufficient exposure with a unilateral or bilateral use of the transverse portion of the full incision. In other words, the lower end of the midline incision is extended transversely from the pubic symphysis to the pubic tubercle, and the ipsilateral rectus sheath and muscle are divided off the pubic crest.

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Appendix B: Canine Osteosarcoma

Charles Kuntz

INTRODUCTION AND USE OF CANINE OSTEOSARCOMA AS A MODEL FOR HUMAN OSTEOSARCOMA (Figure B1A)

Osteosarcoma occurs commonly in the dog. It has been estimated that there are 8000 new cases per year in the United States alone. This high frequency makes it an excellent model for human osteosarcoma and it has frequently been used for this purpose.^{1,2} Similarities between canine and human osteosarcoma include metaphyseal occurrence, typical metastasis to lungs and other bones, and response to doxorubicin and platinum-based protocols. Canine osteosarcoma appears to be more malignant than human osteosarcoma in that, without treatment, death usually occurs within 4–5 months. This offers another advantage when considering it as a model for the human disease. Research protocols very rapidly demonstrate effectiveness of therapeutic attempts. Researchers can frequently demonstrate effectiveness within 2 years of beginning a therapeutic trial. Because financial incentives can be offered clients, identifying candidates has not been a problem. Necropsy compliance is usually very high. Alternatives for treatment can be attempted relatively easily if a therapeutic protocol can be logically justified based on experimental data in other species.

DEMOGRAPHICS AND PRESENTING CLINICAL SIGNS

Osteosarcoma is the most common malignant bone tumor in dogs. There is a biphasic prevalence age distribution curve for canine osteosarcoma, with peaks at 2 and 7 years. A male predominance has been shown in some studies, whereas others have shown no sex predilection. It most commonly occurs in metaphyseal bone. Commonly affected sites, in order of frequency, include the distal radius, proximal humerus, distal ulna, distal femur, proximal tibia, distal tibia, and diaphyseal ulna. Other affected sites include ribs, skull, vertebral bodies, scapula, metatarsal and metacarpal bones, lung, spleen, and mammary tissue. Primary soft-tissue occurrences are rare.^{3,4}

Most affected dogs present with lameness resulting from appendicular osteosarcoma. Usually, a painful swelling is identified over the affected region. Dogs with mandibular and orbital sites may present with dysphagia. Dogs with cranial or vertebral tumors will present with neurologic deficits. Dogs with pelvic masses may present with dyschezia. Some dogs will present with a history of acute exacerbation of clinical signs following trauma. This may mislead the clinician into suspecting a fracture or anterior cruciate ligament rupture. Radiographs of the affected region will usually confirm the diagnosis.

DIAGNOSTIC WORKUP (REGIONAL DISEASE)

Regional radiographs, in addition to predisposing factors such as large breed and advanced age, usually confirm the diagnosis of osteosarcoma and show the tumor's extent in commonly affected anatomic sites. Typical lesions are a mixed pattern of cortical lysis and periosteal proliferation. Although a previous study suggested that radiographs underestimate the local extent of the tumor,⁵ a recent study showed that high-detail radiographs overestimate the local extent of the tumor. Nuclear scintigraphy also overestimates the local extent of the tumor, and to a greater degree than radiographs. Computed tomography is helpful in delineating skull⁶ and thoracic wall tumors.⁷ It can also be used for appendicular tumors to determine the extent of resection required to attain complete surgical margins. Determination of tumor volume and tumor length is of prognostic value in dogs with osteosarcoma in that large tumor size is associated with a poorer prognosis.

Biopsy may be performed, although it is usually not necessary to confirm the diagnosis. If performed, a Jamshidi biopsy needle should be used, and two samples taken, including the center and the periphery of the lesion. If this protocol is followed, a diagnostic accuracy of 90% can be achieved.⁸ Reactive bone may be identified, and this suggests that more aggressive biopsies are indicated.

DIAGNOSTIC WORKUP (METASTATIC DISEASE)

Approximately 10% of dogs will show gross evidence of distant metastasis at the time of diagnosis. Sixty percent will metastasize to lung and 40% will metastasize to other musculoskeletal sites. Thoracic radiographs, including right and left lateral and anterior/posterior, views are performed. Thoracic radiographs are limited in that they delineate only lesions which are greater than 6 mm in diameter. Computed tomography can also be used to screen for thoracic metastasis, but is not widely used. When available, nuclear scintigraphy is also performed, and will show occult bony metastasis in 10% of cases.

TREATMENT OPTIONS

Cure is achieved in less than 15% of dogs diagnosed with osteosarcoma. Treatment is directed at palliating or eliminating locoregional disease and preventing distant metastasis. Preventing of distant metastasis without eliminating the primary tumor offers no survival advantage. Analgesic therapy alone, using aspirin or piroxicam, has a median survival time of 90 days. It is most effective in dogs with relatively small tumors, in the absence of pathologic fractures. Most of these dogs

are euthanized because of pain and/or pathologic fracture of the affected bone. Palliative radiation therapy has also been attempted with coarsely fractionated radiation therapy (24–28 Gy in three or four dose increments). This does appear to reduce bone pain, but does not significantly improve survival. Patients with small tumors in the absence of pathologic fractures appear to have the best survival. The median survival time is 120 days. Most dogs are euthanized because of intractable pain and/or pathologic fracture.

Amputation offers significant improvement in survival over medical management in dogs with appendicular osteosarcoma.⁹ Amputation is well tolerated in almost all dogs in which it is performed, including those who are obese and those with neurological deficits. The author has performed approximately 300 amputations in dogs and has had only one, who had degenerative myelopathy, who had difficulty walking after surgery. This dog eventually was fully ambulatory 40 days after surgery. Most other dogs are fully ambulatory within 3 postoperative days. Regardless of the location of appendicular tumor, all amputations are performed using scapulectomy or coxofemoral disarticulation for front-limb and hindlimb lesions, respectively. Amputation by scapulectomy is associated with better function and cosmesis than amputation by scapulohumeral disarticulation or humeral–antebrachial disarticulation, and is technically less challenging. Coxofemoral disarticulation is also associated with better cosmesis and is also technically less challenging than amputation by midfemoral osteotomy or femorotibial disarticulation. Preservation of the extremity in dogs is not beneficial because they do not tolerate prostheses, and they function well without them. In two surveys, function and client satisfaction were very good to excellent in 98% of pets.¹⁰ Dogs having amputation alone for the treatment of appendicular osteosarcoma have a median survival time of 5 months. These dogs usually die of metastasis.

Rib tumors are treated with thoracic wall resection and, when treated with adjuvant chemotherapy, patients have a median survival time of 1 year. Mandibular tumors are treated with hemimandibulectomy; maxillary tumors are treated with partial maxillectomy and/or orbitectomy. Spinal tumors are treated with decompression and rarely have long-term survival. Pelvic tumors are usually treated with amputation and hemipelvectomy, and these patients usually have excellent function.

Limb salvage surgery can be performed in some dogs with appendicular osteosarcoma (Figures B1A,B and B2A,B).¹¹ Dogs with tumors of the scapula, diaphyseal and distal radius and ulna, metacarpus, metatarsus, diaphyseal humerus, femur and tibia and distal tibia treated with limb-salvage surgery are associated with

good to excellent function. Allograft implantation is not required for tumors of the scapula, metatarsus, metacarpus or ulna (distal or diaphyseal). Most other diaphyseal tumors and tumors of the distal radius treated with limb-salvage surgery require allograft implantation and are associated with good function. Dogs tolerate removal of up to 90% of the scapula with good function. Dogs with tumors of the proximal humerus treated by scapulohumeral arthrodesis following allograft implantation have poor functional outcome.¹² The median survival time in dogs treated with limb-salvage surgery for appendicular osteosarcoma and chemotherapy is equivalent to those treated with amputation and chemotherapy, and is approximately 1 year. There is a 25% local recurrence rate following limb-salvage surgery, and local recurrence does not appear to negatively affect survival. If local recurrence occurs, a second limb-salvage surgery can be attempted, or amputation can be performed.

Allograft implantation usually requires maintenance of a bone bank. Bones can either be harvested sterilely and directly implanted, or harvested cleanly and secondarily sterilized prior to implantation. Transmission of infectious agents from the donor to the recipient has not been a significant problem. Infectious agents are usually introduced during the preparation of the graft, resulting in local infection. Methods for sterilization include steam sterilization, ethylene oxide sterilization and, more recently, low-temperature hydrogen peroxide plasma gas sterilization. Low-temperature hydrogen peroxide plasma gas sterilization does not cause deterioration of biomechanical properties of allograft bone.¹³ The author has performed limb-salvage surgery in two dogs using autograft bone which was autoclaved during the surgical procedure, and reimplanted in the tumor bed, with good results. This offers the advantage of no requirement for a bone bank. The allograft is filled with sterile methylmethacrylate prior to implantation. This has been shown to improve the biomechanical properties of the implant without negatively affecting bone incorporation. Limb-salvage surgery, where an allograft is implanted, is associated with a 50% infection rate. Interestingly, dogs who have a culture-positive infection are associated with a significant improvement in survival (median survival time of 600 days, compared with 290 days in dogs not having postoperative infection).

ADJUVANT CHEMOTHERAPY

Chemotherapy significantly improves survival in dogs with appendicular osteosarcoma when locoregional disease is eliminated using surgery. Protocols which have shown significant improvement in survival include doxorubicin,¹⁴ cisplatin,^{15,16} carboplatin,¹⁷ and to

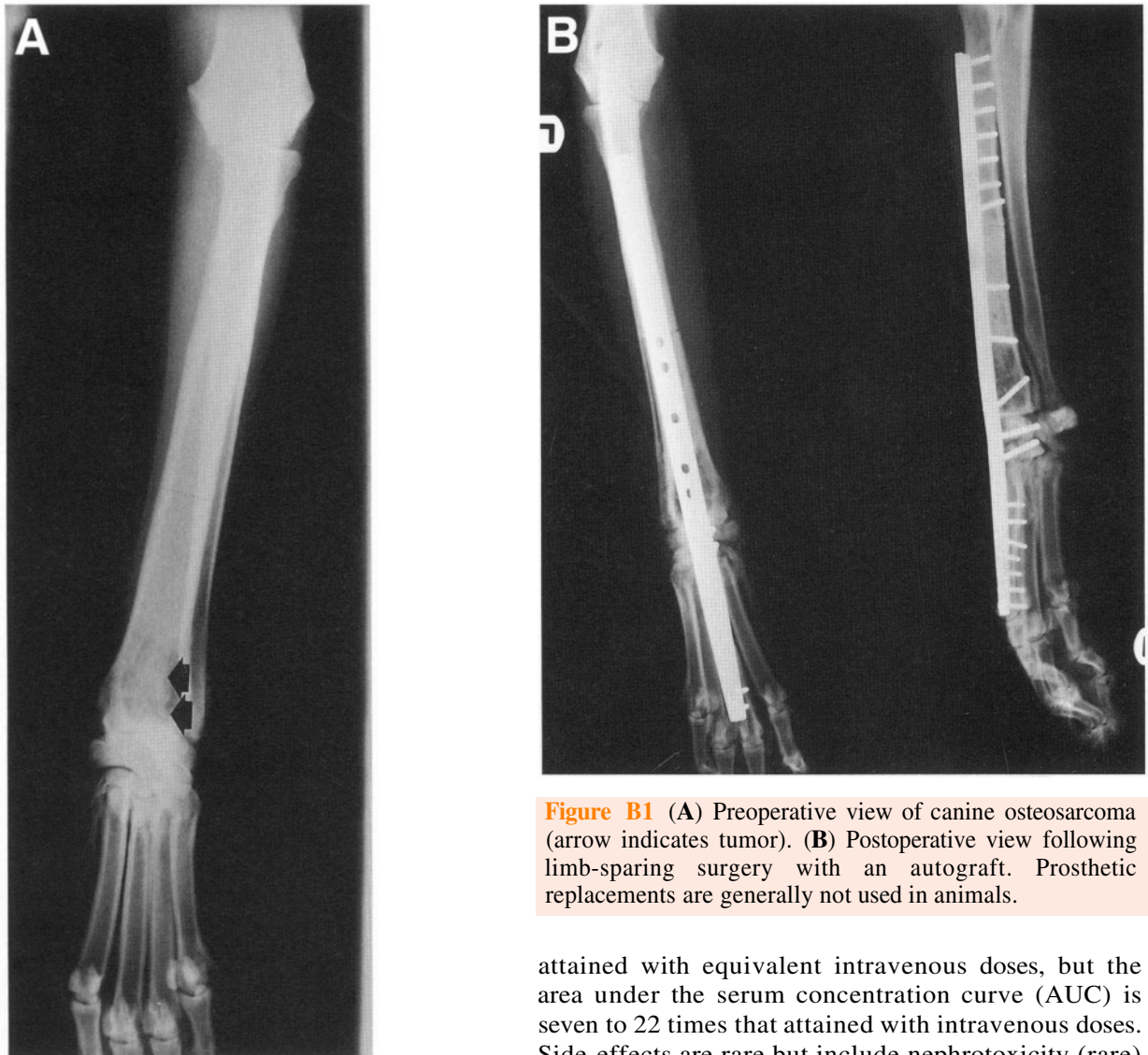


Figure B1 (A) Preoperative view of canine osteosarcoma (arrow indicates tumor). (B) Postoperative view following limb-sparing surgery with an autograft. Prosthetic replacements are generally not used in animals.

a lesser extent, loboplatin.¹⁸ The median survival times for the former three is approximately 1 year, and for the latter, 7 months. There has been no advantage to combination chemotherapy demonstrated. Dogs usually are euthanized because of the development of distant metastasis. Chemotherapy is well tolerated in most dogs. Eighty percent of dogs complete the course of chemotherapy without any significant side-effects. Eighteen percent have mild side-effects including bone marrow suppression, and gastrointestinal complications. Two percent have side-effects significant enough to require hospitalization.

Implantable cisplatin chemotherapy has been used to treat dogs with osteosarcoma,¹⁹ with encouraging results. Cisplatin is invested in a polylactic acid polymer which allows gradual release of the cisplatin over approximately 3 weeks. Peak levels, commonly associated with side-effects, are 10–30% of those

attained with equivalent intravenous doses, but the area under the serum concentration curve (AUC) is seven to 22 times that attained with intravenous doses. Side-effects are rare but include nephrotoxicity (rare) and infection (common). Infection of the chemotherapy site appears to offer protection against metastasis, similar to that seen with infected limb-salvage allografts. The chemotherapy takes the form of a sponge which is implanted in the amputation stump or limb-salvage tumor bed, or of a gel which is a liquid at room temperature and becomes a solid at body temperature. Implantation of sponges in the limb-salvage tumor bed also reduces the incidence of local recurrence.

PROGNOSIS

Tumor size, calculated as the percentage of bone length affected by tumor, or as an actual tumor volume, has been found to be prognostic in dogs with osteosarcoma. Larger tumors have been found to have a poorer prognosis. Anatomic site is also prognostic in that appendicular osteosarcoma (radius, ulna, humerus, femur and tibia) is associated with a median survival

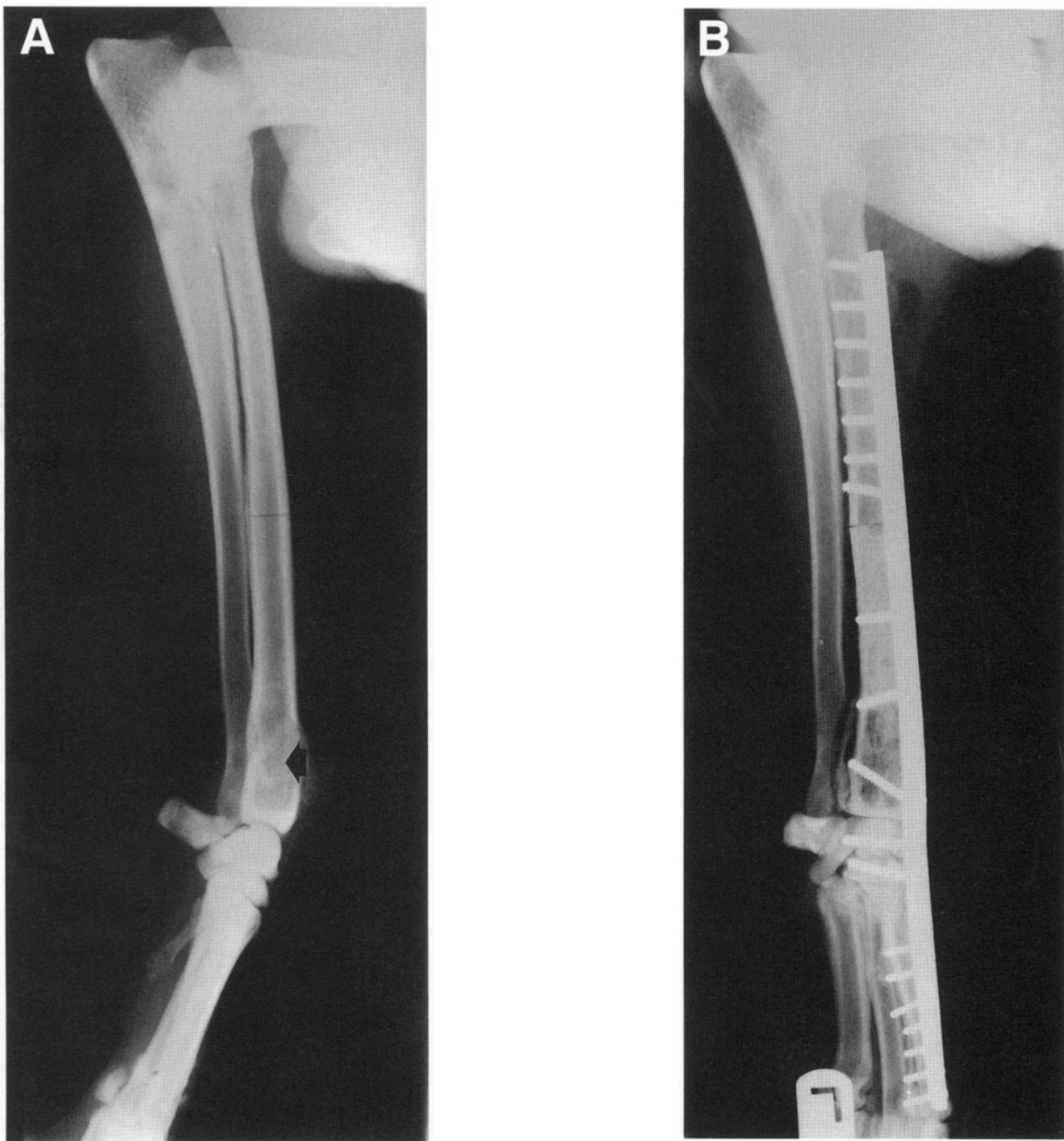


Figure B2 (A) Preoperative view showing an osteosarcoma (arrow) of the distal radius. (B) Postoperative view of the same patient.

time of 1 year when treated with aggressive surgery and chemotherapy. Tumors of the mandible and scapula have a slightly better prognosis with a median survival time of about 15–18 months. Tumors of spine and skull have a poorer prognosis because of anatomic limitations on aggressive surgical resection. Extraskelatal osteosarcoma has a dismal prognosis with a median survival time of 73 days.^{3,20–25} The bone isoenzyme of alkaline phosphatase has been shown to be prognostic in that high levels before surgery are associated with a

poorer prognosis. After the initial decrease following surgery, an increase helps predict impending gross metastasis. Quantification of metalloproteinases two and nine have shown some predictive value, and further studies are under way. Recent studies have suggested that tumor grade, characterized by degree of necrosis, mitotic rate and cell differentiation, is highly prognostic; further study is necessary.¹⁸

CONCLUSION

Osteosarcoma is a common tumor in the dog. It serves as an excellent model for human osteosarcoma studies.

It is malignant, and affected patients usually die of their tumors. Aggressive surgery and chemotherapy have been shown to significantly improve survival.

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